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PATHOGENESIS OF PASSIVE RH ISOSENSITIZATION IN THE NEWBORN (ERYTHROBLASTOSIS FETALIS)

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THE DISCOVERY by Levine[1] of the immunologic relationship between the Rh factor in the erythrocytes of the fetus and the formation of anti–Rh antibodies in the Rh–negative mother has been of the greatest importance in the understanding of that group of familial conditions in the newborn characterized by destruction of the red cells. On the basis of this explanation, however, certain assumptions arrived at by inference rather than by critical analysis of clinical studies have been made by many concurring writers. It is assumed, for instance, that hemolysis and agglutination produced by antibodies transferred from the mother to the fetus by way of the placenta are responsible for all ensuing organic damage, either through anoxemia due to anemia or through the overproduction of the products of erythrocyte destruction. Injury to the liver, when mentioned at all, is not considered as a primary pathologic process but is presumed to be secondary to damage by the anemia, by the pressure of masses of extramedullary hemopoietic cells which are also "compensatory to the hemolysis" or by the hemosiderosis and "bile thrombi" formed as the result of accumulations resulting from the destruction of red cells. Edema and purpura are likewise considered to result from the anemic anoxemia. The great variation in severity manifested in the various forms of the disease, assumed formerly to be correlated with the number of agglutinating antibodies contained in the mother's serum

From the Women and Children's Hospital.

1. Levine, P.: The Role of Isoimmunization in Transfusion Accidents in Pregnancy and in Erythroblastosis Fetalis, editorial, Am. J. Obst. & Gynec. **42**:165 (July) 1941. Levine, P.; Katzin, E. M., and Burnham, L.: Isoimmunization in Pregnancy: Its Possible Bearing on the Etiology of Erythroblastosis Fetalis, J. A. M. A. **116**:825 (March 1) 1941. Levine, P.: The Role of Isoimmunization in Transfusion Accidents and in the Pathogenesis of Erythroblastosis Fetalis, editorial, Am. J. Clin. Path. **11**:898, 1941.

and thence delivered, presumably, to the fetus in whom hemolysis is then supposed to occur, is now related to the concentration of "blocking antibodies."[2] Later pregnancies are presumed to result in more severely affected infants because of the increment in production of antibodies in the mother expected with each pregnancy, while the period of time during which the fetus is exposed to the transfer of antibodies is regarded as crucial.

The plausibility of these hypotheses, together with the fact that they are undoubtedly in part true, leads to oversight of certain clinical features of this disease which cannot be understood if hemolysis is the only pathologic process resulting from the antigen–antibody reaction in the affected child. The cases presented in this paper have been chosen because they exhibit outstanding features not wholly explainable by the currently accepted ideas or because they suggest an alternative concept which does not contradict but rather complements the isoimmunization theory of Levine.

FAMILY "D": (CASES ONE AND SIX)

CASE 1 (patient of Dr. Maude Winnett and of Dr. Joseph Brennemann, who supplied protocols and histologic sections).—This was the third child. He was born at Grant Hospital in 1935 and seemed normal and vigorous at birth. Jaundice developed within the first twenty-four hours. A blood cell count and a differential count on the second day revealed the typical blood picture of erythroblastosis fetalis. The liver and the spleen were enlarged. The baby was deeply jaundiced and listless and had a weak cry. Transfusions of 60, 80 and 100 cc. of compatible citrated blood were given by vein on the second, the seventh and the tenth day, respectively. He was given feedings of expressed breast milk from his own mother. There was no spasticity of the muscles of the neck or the extremities. By the fifteenth day he was much improved, the jaundice was less pronounced, he was taking breast feedings well and he was gaining weight steadily. Blood cell counts, repeated twice weekly, are recorded in table 1. When he was 3½ weeks of age the prick for the blood cell count bled for two hours, and when he was 4 weeks of age the puncture wound bled intermittently for two days. At 5 weeks of age, twenty-five days after the last transfusion, he suddenly seemed to be in severe colicky pain during the night. Several small stools were passed. His crying became rapidly weaker with a squeaky quality, and alternated with periods of labored breathing with expiratory grunts. The fontanelle at this time was depressed. The next day he refused or was unable to take feedings or fluids and vomited several times. There was increasing pallor and stupor. The fontanelle became tense. He was admitted to Children's Memorial Hospital, where lumbar puncture released grossly bloody spinal fluid under increased pressure. Hematemesis occurred repeatedly and frequent tarry stools were passed. Convulsive movements and bilateral clonus of the ankles developed. The temperature during the last thirty-six hours rose to 102 F. He died on the fifth day following the onset of the acute symptoms, at the age of 5½ weeks.

A complete necropsy was performed. A condensed report is as follows: A greenish yellow tinge was present over the entire surface of the skin. The

2. Diamond, L. K., and Denton, R. L.: The Treatment of Erythroblastosis Fetalis, J. A. M. A. **128**:686 (June 30) 1945.

edge of the liver was palpable 3 cm. below the costal margin, and the spleen 1 finger below the ribs. The umbilicus was well healed. The blood showed a remarkable fluidity. The lungs were fully expanded. They were pale pink, with scattered irregular areas of darker red, measuring 2.0 to 4.0 mm., which appeared on the pleural surfaces. When the pulmonary tissue was exposed by section with a knife, the lung was seen to be uniformly air bearing and pale pink. Here and there were irregular, deep red, hemorrhagic foci, similar to those observed on the pleural surface.

The liver and the spleen were grossly enlarged. The liver was dark green and firm and weighed 180 Gm. The biliary passages were demonstrably patent. The stomach was distended, and from the serosal aspect, seen through the translucent wall, the viscus appeared to contain dark fluid. When the stomach was incised, a large amount of greenish black, coffee ground liquid was liberated.

TABLE 1.—*Hematologic Data in Case 1*

Date *.....	7/22	7/23	7/25	7/26	7/30	7/31	8/2	8/5	8/8	8/12	8/16
Hemoglobin, percentage.....	70	69	64	66	88	98	86	..	74	96	86
Red blood cells, millions.....	3.4	3.24	2.35	2.98	3.78	3.89	3.76	3.12	3.0	4.01	3.34
White blood cells.....	21,300	20,100	14,850	16,400	16,400	17,500	15,600	18,400	19,350	21,100	16,200
Normoblasts/ 100 white blood cells.....	32	..	1	8	2	..	3	8	12	..	1
Polymorphonuclear cells.....	47	..	36	38	52	40	28	26	38	30	29
Metamyelocytes	..	..	..	..	1	4	..	..	..	..	..
Myelocytes.....	3	..	..	..	..	..	..	..	..	..	..
Eosinophils.....	7	..	12	12	5	5	..	3	4	3	7
Basophils.....	2	..	..	..	..	2	5	1	..	1	2
Lymphocytes...	21	..	47	36	10	24	20	25	19	12	15
Monocytes.....	20	..	4	13	32	24	47	44	38	54	47
Irritation forms	..	..	1	1	..	1	..	1	1		
Platelets.....	..	..	..	..	216,000	..	..	..	..		
	Marked polychromasia and macrocyrosis		..	..	Anisocytosis polychromasia		Marked monocytosis with young forms				
Transfusion....	60 cc.	..	80 cc.	100 cc. (July 28)							

* 1935.

There were no ulcerations. Gross lesions or bleeding points could not be detected. The small bowel was filled with material similar to the stomach contents, and a large quantity likewise distended the colon. No source of gross hemorrhage was evident.

The urinary bladder was contracted, and the mucosa was thrown into many folds. It contained from 5 to 10 cc. of thin clear greenish yellow urine. The vertebral marrow was red and abundant.

When the dura over the right temporal lobe was incised, a quantity of thin red blood flowed out. When the occipital lobe was exposed large clots were released. On removal of the brain, an irregular, lumpy hemorrhagic mass dropped from the superior surface of the right parietal lobe, exposing a large ragged defect in the substance of the brain opening into the right ventricle.

Histologic Examination.—Lungs: There were focal hemorrhages in some of the pulmonary sections. The alveolar septums were thickened and cellular. In some places the proliferation of these cells was so dense as to produce moderate encroachment on and obliteration of some of the alveolar spaces. In the larger

blood vessels there was some proliferation of the vascular endothelium which thus appeared to be several layers in width.

Liver: The Kupffer cells were swollen with ingested blood pigment and were clearly demarcated in contrasting colors lining the hepatic sinusoids. The hepatic cells were swollen and speckled with coarse, brown granules. Many of the canaliculi were occluded by bile thrombi. Here and there were tiny, discrete collections of large, pale cells with voluminous central nuclei containing a heavy network of chromatin. Many nucleated erythrocytes were circulating within the distended sinusoids. Many of the hepatic cords were somewhat atypical in arrangement, suggesting the presence of actively regenerating tissue.

Spleen: The follicles were large, compact and distributed in a pulp that contained many red cells, normoblasts and pigment-laden macrophages.

The kidney showed a moderate degree of parenchymatous degeneration.

The pancreas, the stomach and the colon were normal.

Pathologic Diagnosis.—The pathologic diagnosis was erythroblastosis fetalis; ectopic foci of erythropoiesis in the lungs, the liver, the spleen, the thymus and the lymph nodes; massive intracranial hemorrhage; degeneration of the right

TABLE 2.—*Oxygen Content and Capacity of Cord Blood (Case 6) and of Mother's Venous Blood*

Source of Blood	Content (Volumes per Cent)	Capacity (Volumes per Cent)	Percentage of Saturation
Umbilical vein (2 samples).....	12.34	17.03	
	12.70	17.30	72.3
Mother's vein.....	17.63	19.17	
	18.09	19.17	93.0

parietal lobe; multiple discrete hemorrhages into the lungs and the liver; subendocardial petechiae in the left auricle; subperiosteal hemorrhage of the right sixth rib; biliary cirrhosis of the liver (?), and generalized icterus of skin and viscera.

CASE 6 (patient of Dr. Josephine Chapin).—The next child was born in 1941, at the Women and Children's Hospital. Estimations of the oxygen in the blood of the umbilical vein, drawn anaerobically before section of the cord, were made by Miss Martha Janota, of the Department of Chemistry of Michael Reese Hospital, with the results listed in table 2. The number of nucleated red cells per cubic millimeter (table 3) was just over the limit of normal suggested by Hawksley and Lightwood.[3] While the oxygen capacity was considerably under the normal for fetal blood found by Eastman [4] (average, 20.8), the oxygen content of the blood of the umbilical vein was higher than most of the values found by Eastman (average, 10.5). This high value for oxygen content may be due in part to the fact that the mother breathed deeply and rapidly just before and during delivery. This resulted in a high percentage of saturation of her (venous) blood. These observations suggest a correlation between the mildness of the erythroblastemia and the oxygen saturation of the infant's blood.

Jaundice was not present at delivery, but could be detected within one hour. After a blood cell count at 1 hour of age the infant was given 80 cc. of pooled

3. Hawksley, J. C., and Lightwood, R.: A Contribution to the Study of Erythroblastosis: Icterus Gravis Neonatorum, Quart. J. Med. **3**:155 (April) 1934.

4. Eastman, N. J.: Foetal Blood Studies: I. The Oxygen Relationships of Umbilical Cord Blood at Birth, Bull. Johns Hopkins Hosp. **47**:221 (Oct.) 1930.

plasma intravenously. Oxygen was administered for fifteen minutes eight times daily. By the end of the first day the jaundice had deepened considerably, the hemoglobin was 90 per cent, the red cell count was 4,040,000 and, although the condition of the child had deteriorated, she was again given an intravenous

TABLE 3.—*Hematologic Studies of First Two Days (Case 6)*

Blood	Cord	One Hour	End of First Day	End of Second Day
Icterus index	32	—	190	—
Direct van den Bergh reaction	Faint; delayed	—	Immediate; moderate	—
Indirect van den Bergh reaction	Immediate; moderate	—	Immediate; moderate to strong	—
Red blood cells, millions	2.76	4.56	4.04	3.32
Nucleated red blood cells	5,160	5,580	1,140	250
Hemoglobin, percentage	60	90	90	84
White blood cells	15,640	21,320	25,860	24,850
Fragility:				
Partial	0.42%			
Complete	0.30%			
Condition of infant	Good; not jaundiced	Good; slightly jaundiced	Fair; deeply jaundiced	Poor; very deeply jaundiced
Procedure	Mother breathed deeply	Plasma, 80 cc. intravenously	Plasma, 80 cc. intravenously	Citrated blood 100 cc. intravenously
		Oxygen given 15 minutes 8 times daily		
Blood group O		Father: A Rh_1 positive; mother: O Rh negative		

TABLE 4.—*Blood Counts and Hemoglobin Estimations (Case 6)*

Date, 1941	Red Blood Cells, Millions	Nucleated Cells	Nucleated Red Blood Cells	White Blood Cells	Hemoglobin, %	Comment
9/21	2.76	20,800	5,160	15,640	60	33 nucleated red blood cells/100 white blood cells in cord blood
9/21	4.56	26,900	5,580	21,320	90	26 nucleated red blood cells/100 white blood cells; at end of first hour 80 cc. pooled plasma intravenously
9/22	4.04	27,000	1,140	25,860	90	80 cc. pooled plasma intravenously
9/23	3.22	25,100	250	24,850	85	100 cc. citrated blood intravenously; 5 cc. of 10% calcium gluconate
9/24	4.04	13,000	0	13,000	95	100 cc. citrated blood intravenously
9/25	6.18	—	0	12,900	100	5% dextrose subcutaneously, 40 cc. twice daily
9/29	3.14	—	0	16,050	73	Coagulation time: 20 sec.; bleeding time; 1½ min.
9/30	2.92	—	0	26,050	70	125 cc. citrated blood intravenously
10/ 6	4.34	—	0	15,900	84	Jaundice completely gone; patient at home
10/16	3.19	—	0	12,600	74	
11/17	3.82	—	0	13,150	76	
12/ 7	4.46	—	0	8,830	76	12 weeks old

transfusion of 80 cc. of pooled plasma. The following day the jaundice continued to deepen. By the end of the second day, although the hemoglobin content was 84 per cent and the erythroblastemia had practically disappeared, the infant appeared definitely to have become worse. The jaundice was more noticeable than on the preceding day when the icterus index had been 190, and the infant was listless and was taking fluids poorly. It was deemed inadvisable to continue

further with plasma, as the evidence for increasing hepatic injury seemed unequivocal. She was given a transfusion, therefore, of 100 cc. of Rh-positive compatible blood, followed by 5 cc. of a 10 per cent solution of calcium gluconate. A second transfusion of 100 cc. of blood from the same donor was given twenty-four hours later. Subcutaneous injections of 5 per cent solution of dextrose in amounts of 40 cc. twice daily were continued through the thirteenth day. By the tenth day the red cell level had fallen to 2,900,000. The infant was taking her feedings well, and the icteric color was lessening daily. A third transfusion of 125 cc. of blood from the same donor was given after repeating the cross matching. After this the jaundice cleared completely, and it had entirely disappeared by the fifteenth day, when she was discharged from the hospital. Recovery thereafter was uneventful. At 6 months of age the infant was crawling and could pull herself to a standing position without aid.

The mother was found subsequently to have type O Rh-negative blood, the father type A Rh_1 Hr-negative blood, and the donor whose blood was used exclusively had type O Rh_1 blood.[5] The child has type O Rh-positive blood.

FAMILY "B" (CASE TWO)

The first two pregnancies resulted in the birth of normal, healthy children. The third child died on the thirteenth day of life with jaundice of unknown origin.

CASE 2.—Delivery of the fourth child occurred at the Women and Children's Hospital in February 1937. The child appeared normal, alert and vigorous after a normal and easy birth. The cord blood showed a positive direct van den Bergh

TABLE 5.—*Studies of Infant's Cord Blood and of Father's and Mother's Blood (Taken at Time of Delivery) (Case 2)*

	Blood of Infant's Cord	Mother's Blood	Father's Blood
Icterus index	21	8	8
van den Bergh reaction:			
Direct	+	0	0
Indirect	+	Ft. +	Ft. +
Erythrocyte fragility, percentage:			
Partial hemolysis	0.32	0.42	0.40
Complete hemolysis	0.22	0.30	0.30
Hemolysis of cord:			
Erythrocytes with mother's serum	0		
Erythrocytes with father's serum	0		

reaction, which indicated that hepatic complications were present before birth, at a time when the bilirubin content of the blood was not yet greatly elevated (icterus index 21) and jaundice was absent or subliminal. Within one hour the skin of the face was observed to be definitely bronzed. Ten hours later the jaundice was general. The child was lethargic at this time and hyperirritable when moved, with tremors of the arms and slight clonus of the legs and the feet. The edge of the liver was palpable 2 fingerbreadths and the spleen 1½ fingerbreadths below the costal margins. Hematologic observations showed a mild anemia, with

5. These bloods were typed in the laboratory of Dr. I. Davidsohn, who assisted in this and in a following case.

36 nucleated red cells per hundred leukocytes. The leukocytes were increased, with a shift to stab cells and young forms. The clinical picture and the hematologic observations indicated erythroblastosis fetalis. It was decided to give no blood, breast feedings or milk from the baby's own mother.

When the infant was 14 hours of age a smear revealed 58 nucleated red cells per hundred leukocytes; pallor was more noticeable, and a slight pitting edema was present over the lower extremities. At this time 65 cc. of compatible blood from the maternal grandmother was given intravenously. Oxygen was given for fifteen minutes six times daily. The jaundice deepened through the following day, although the infant seemed improved. On the third day, however, the skin had become more deeply icteric, and the infant was again listless and hyperirritable and appeared toxic. Because of the "toxic" appearance, and in spite of an erythrocyte level of 4,360,000, a second transfusion was deemed advisable, and 75 cc. of blood from the maternal grandmother was again given intravenously, followed

TABLE 6.—*Blood Counts and Hemoglobin Estimations (Case 2)*

Date, 1937	Red Blood Cells, Millions	Nucleated Red Blood Cells per 100 White Blood Cells	Reticulocytes	White Blood Cells	Hemoglobin, %	Comment
2/12	3.27	36	17%	20,990	—	Data secured before 1st transfusion (65 cc.)
2/13	4.43	12	....	33,600	85	
2/14	4.36	8	....	16,900	80	Data secured before 2d transfusion (75 cc.)
2/16	4.0	0	....	24,600	75	
2/19	2.10	0	....	19,350	60	Data secured before 3d transfusion (35 cc.)
2/21	2.86	0	....	16,200	60	
2/22	1.70	0	1%	13,700	55	Data secured before 4th transfusion (75 cc.)
2/24	4.10	0	....	18,500	80	
3/ 4	3.06	0	....	9,700	60	
3/18	2.79	0	....	10,630	60	Coagulation time: 2 min.; bleeding time 1½ min.
3/25	2.83	0	....	9,950	52	6 weeks old
4/ 5	3.07	0	....	5,850	55	
4/15	3.61	0	....	10,350	65	9 weeks old

by 5 cc. of 10 per cent solution of calcium gluconate. Following this the clinical improvement was much more noticeable than before, and the child presented no further signs of intoxication, although anemia recurred. Dextrose was administered subcutaneously through the eighth day, when the jaundice had almost disappeared. On the twelfth day the erythrocyte level had dropped to 1,700,000 per cubic millimeter, with a hemoglobin content of 55 per cent. The baby was lively, ate well and seemed entirely normal except for the pronounced pallor. The reticulocyte count was 1 per cent, and there were no nucleated red cells in the blood smear. The edge of the liver was at the costal margin, and the spleen was not palpable. On the thirteenth day a fourth transfusion of 75 cc. of blood from the maternal grandmother was given after cross matching. The infant continued active and vigorous, although the red cell count, after an initial rise to 4,100,000, again began to fall. When the infant was 9 weeks of age the red cell count was 3,610,000 and the hemoglobin content was 65 per cent. When seen at 11 months of age the child seemed somewhat accelerated in coordination and mental development.[6]

6. Dr. Katherine Howell assisted and gave helpful suggestions in this and in the 2 preceding cases presented.

This family moved from the city and could not be located subsequently, so that the Rh status of its members could not be determined. The father belonged to blood group 0, and the baby, the mother and the grandmother to blood group B.

FAMILY "H" (CASE ELEVEN)

The first child, now 8 years of age, is spastic and considerably retarded in mental development. The next two pregnancies resulted in stillborn infants, both "very large"; no necropsy was performed on either.

CASE 11 (patient of Dr. Clementine Frankowski).—The fourth child was born on July 18, 1944, at St. Catherine's Hospital, East Chicago. The infant seemed normal at birth, but jaundice and deeply colored urine were noted on the second

TABLE 7.—*Blood Counts and Hemoglobin Estimations (Case 11)* *

Date, 1944	Red Blood Cells, Millions	Nucleated Cells	Nucleated Red Blood Cells	White Blood Cells	Hemoglobin, %	Comment
7/21	2.88	19,050	8,640	10,410	60	Data secured before 1st transfusion (100 cc. Rh-positive blood; 5 cc. 10% calcium gluconate intravenously)
7/23	3.54	13,700	.....	.....	79	75 cc. Rh-positive blood intravenously
7/24	3.64	7,000	458	6,542	73	
7/25	3.63	12,900	0	12,900	71	90 cc. Rh-positive blood intravenously
7/28	4.10	15,650	0	15,650	85	
8/ 4	3.40	—	0	15,550	71	
8/15	2.59	—	0	14,250	50	4 weeks old
8/22	1.49	—	0	5,100	48	130 cc. Rh-positive blood
10/11	3.34	—	0	8,350	69	12 weeks old
11/ 7	4.27	—	0	8,600	79	Weight 18 lb. 15 oz. (8,590 Gm.)

* Length of labor was two hours and fifty-eight minutes, and weight at birth was 6 lb. 11 oz. (3,033.4 Gm.).

day. The jaundice had become much more intense by the third day, and a blood cell count revealed 2,880,000 erythrocytes with a hemoglobin content of 60 per cent and 83 nucleated red cells per hundred leukocytes. The mother's blood was of type A and Rh negative, and the baby's of type A and Rh positive. The feeding of the mother's milk was stopped at once. When seen on the evening of the third day the skin presented a deep lemon yellow color and the scleras were icteric. The edges of the liver and the spleen were felt 2½ fingerbreadths below the costal margins. The baby was apathetic, but appeared hyperirritable on handling. There was no spasticity of the extremities. The infant was given 100 cc. of Rh-positive compatible blood and 5 cc. of 10 per cent solution of calcium gluconate intravenously with immediate clinical improvement. Oxygen and subcutaneous injections of 5 per cent solution of dextrose were employed as usual. Further transfusions of 75 and 90 cc. of Rh-positive blood were given on the fourth and the seventh day, respectively. The jaundice disappeared rapidly. At 5 weeks of age the infant was pale but strong and active. She had made excellent gains in weight. There was no enlargement of the liver or the spleen. There were no nucleated red cells and no toxic leukocytes in the blood smear. The red cells had dropped to 1,490,000. She was given 130 cc. of Rh-positive blood intravenously. At 2 years of age she was entirely normal and thriving.

FAMILY "J" (CASE TWELVE)

CASE 12 (patient of Dr. Clementine Frankowski).—The second child was born on Oct. 11, 1944, at St. Catherine's Hospital, East Chicago. Outlet forceps were employed. Oxygen was administered for a time after delivery, and the color and the cry were both noted as good. Jaundice first appeared on the third day and was regarded as physiologic. A blood count revealed 4,780,000 erythrocytes, 8070 leukocytes and 80 nucleated red cells per cubic millimeter. The hemoglobin content was 96 per cent. There was difficulty in getting the infant to take breast feedings, but on the fifth day he nursed vigorously for twenty minutes at 6 p. m. After the feeding at 10 p. m. the nurse noted that he did not "curve into" her arm when she was returning him to the nursery. It was then noted that he held his head rigidly.

When seen at the end of the sixth day the infant was considerably jaundiced. The head was turned slightly to the left and strongly retracted. The arms were

TABLE 8.—*Blood Counts and Hemoglobin Estimations (Case 12)*

Date, 1944	Red Blood Cells, Millions	Nucleated Cells	Nucleated Red Blood Cells	White Blood Cells	Hemoglobin, %	Comment
10/14	4.78	8,150	80	8,070	96	1 nucleated red blood cell/100 white blood cells
10/18	4.07	—	0	17,250	81	Given transfusion of 95 cc. Rh-positive citrated blood
10/19	4.67	—	0	10,800	91	
10/20	....	.....	..	.....	..	Given transfusion: 85 cc. Rh-positive blood
10/23	5.13	—	0	12,500	107	
10/26	....	.....	..	.....	..	Jaundice entirely cleared
10/30	4.89	—	0	14,600	99	Oxygen stopped
11/ 8	4.46	—	0	16,600	..	Toxic granules in leukocytes
11/10	....	.....	..	.....	..	Given transfusion: 100 cc. Rh-positive blood
11/11	4.73	—	0	15,200	93	
11/27	4.08	—	0	13,600	82	
12/14	2.90	—	0	9,000	58	Monocytes: 30/100 leukocytes
1/ 3	3.11	—	0	11,750	60	
3/ 1	3.90	—	0	14,100	73	

strongly flexed and were extended with difficulty. The fists were tightly clenched. The back was rigid and arched slightly backward. Even the gentlest handling evoked a shrill cry. The fontanelle was slightly depressed. The edge of the liver was 1½ fingerbreadths and the spleen 2 fingerbreadths below the costal margins, and the skin was yellow-bronze. A tentative diagnosis of nuclear icterus was made. The infant was given 5 cc. of a 10 per cent solution of calcium gluconate intramuscularly. Oxygen was administered continuously, and 5 per cent solution of dextrose was given daily by hypodermoclysis. Further mother's milk was withheld. Blood counts and transfusions are listed in table 8. The icterus index of blood withdrawn just prior to the first transfusion was 180; the total serum protein was 3.94 mg. and the nonprotein nitrogen 24.7 mg. per hundred cubic centimeters of whole blood.

The mother's blood tested by Dr. Irene Shmigelsky was found to be Rh negative. On the fourteenth day after delivery, blood from the mother, the father and the child was sent to Dr. I. Davidsohn. He confirmed the fact that the mother's blood was Rh negative and reported a weak titer of maternal isoagglutinins. The baby's blood was Rh positive, as was the father's blood.

The jaundice disappeared and the size of the liver and the spleen returned to normal after a second transfusion of 85 cc. of Rh-positive blood on the ninth day. No effect was noted on the spasticity of the extremities, however. On the thirtieth day a third transfusion of 100 cc. of compatible, Rh-positive blood was given by vein, and the baby was discharged from the hospital. The child grew normally in stature, but the spasticity remained and the child did not show a normal development of personality and mentality.

When the child was 5½ months of age a respiratory infection developed which resulted in death from pneumonia. On necropsy the lungs were found to have focal areas of consolidation, most pronounced in the left lung. The bronchi contained frothy fluid. The skull was slightly flattened on the left posterior aspect. The brain was soft and weighed about 700 Gm. The meninges over the left hemisphere were injected. The ventricles were slightly dilated. Sections of the right frontal lobe, the left central ganglions, the cerebellum, the pons and the medulla revealed no abnormal changes with hematoxylin and eosin stain. The bone marrow from the right femur showed normally active granulopoiesis but diminished erythropoiesis. The heart, the liver and the kidneys revealed cloudy swelling. No hemopoiesis was observed in these organs. The pathologic diagnosis was focal bronchopneumonia of both lungs, hyperemia and edema of the brain, cloudy swelling of the myocardium, the liver and the kidneys; infectious softening of the spleen, and clinical recovery from erythroblastosis fetalis.

COMMENT

In their clinical course cases 2 and 11 are typical of most of the cases in which treatment was given which we have observed. They have been included primarily to illustrate the innocuous character of the uncomplicated anemia which still recurs after treatment has eliminated all symptoms ascribable to hepatic injury or anoxia. Erythrocyte levels of 1,700,000 and 1,490,000, respectively, were not accompanied by erythroblastemia, by demonstrable organic damage or by any clinical evidence of intoxication or anoxia. No toxic granules were seen in the leukocytes. There was no jaundice, no edema and no purpura. Bleeding and coagulation times were normal. The liver and the spleen had receded to normal size. The erythrocytes alone were being destroyed, presumably by the specific antibodies, but this destruction was accompanied by no other adverse effect. This lack of correlation between the degree of anemia and the amount and seriousness of hepatic or other organic impairment is strong evidence against anemia's being other than a minor contributory cause of such damage in erythroblastosis fetalis. In cases 2 and 11 this recurrent, uncomplicated but progressive anemia appears to be the result of a true and relatively harmless immune reaction.

In case 6, on the other hand, with an erythrocyte level of 4,000,000 or over, and notwithstanding the intravenous administration of 80 cc. of pooled plasma, unmistakable signs of increasing hepatic injury developed during the first day of life. The icterus index rose from

32 to 190. The direct van den Bergh (qualitative) reaction changed from a "faint, delayed" to an "immediate, moderate" response. After the second administration of plasma the jaundice deepened further. The intensification of the jaundice was not the consequence of hemolysis of transfused Rh-positive cells in this case or a result of destruction of the baby's own Rh-positive cells alone. Hepatic damage is clearly indicated. This injury to the liver cannot be ascribed to anemia, and it can scarcely be ascribed to erythroblastemia. Was it due, then, to obstruction by the accumulation of bile pigment in the liver as the result of the destruction of red cells? In another case we observed clay-colored, bile-free stools and urine showing bilirubin but no urobilin at one stage of the disease. This suggests that an intrahepatic, biliary obstruction may contribute to the production of the jaundice in this disease. But the positive direct van den Bergh response shown by the cord blood in case 2, when the icterus index was only 21, does not support the assumption that biliary obstruction causes the initial injury to the liver. Rather it indicates that the hepatic injury is primary and that inspissated or sluggishly flowing bile is an effect rather than a cause of this damage. The liver is too often ignored by the enthusiastic proponents of the "hemolytic disease" hypothesis. I. A. Abt [7] has stated that "an organic inferiority of the liver itself" seems to be the underlying cause of familial jaundice of the newborn. Javert [8] has also considered the liver an important factor in erythroblastosis neonatorum, and Davidsohn [9] has given the liver a central and important place in his diagram illustrating the production of the disease complex. Emphasis on this organ is certainly justified in case 6, in which the liver appears to be more seriously affected than the erythrocytes. If the demonstrated hepatic injury may not be ascribed to anemia or erythroblastemia in case 6 or, at least initially, to overproduction of bilirubin in case 2, it seems necessary to look for still another mechanism to account both for this and for the various other forms of organic damage in this disease. An interpretation of isosensitization which accounts for the many puzzling clinical observations offers a possible solution.

The antierythrocyte antibodies commonly demonstrated in the laboratory are those producing agglutination and hemolysis, but in Rh sensitization there is a probability of still other antibody effects, as pointed

7. Abt, I. A., in discussion on Dunham, E.: Severe Jaundice in the Newborn, Am. J. Dis. Child. **40**:671 (Sept.) 1930.

8. Javert, C. T.: (*a*) Erythroblastosis Neonatorum: An Obstetrical-Pathological Study of Forty-Seven Cases, Surg., Gynec. & Obst. **74**:1 (Jan.) 1942; (*b*) Further Studies on Erythroblastosis Neonatorum of Obstetric Significance, Am. J. Obst. & Gynec. **43**:921 (June) 1942.

9. Davidsohn, I.: The Rh Factor, M. Clin. North America **28**:232 (Jan.) 1944.

out by Koucky.[10] Wiener[11] and Race[12] have discovered "blocking" or "incomplete" antibodies which inhibit the agglutinating antibodies. More recently Wiener has found further evidence of Rh sensitization by means of the conglutination test,[13] and these "glutinins" may be present with or without demonstrable agglutinins or blocking antibodies. Furthermore, the increased activity of opsonins in passive isoimmunization of the newborn seems clearly indicated not only by engorged macrophages but also in the humoral erythrophagocytosis by monocytes observed in cases of congenital anemia.[14] (The pronounced monocytosis in case 1 may be noted in this connection.) Indeed, the tremendous phagocytosis of red cells and their pigmented fragments, especially in the Kupffer cells of the liver and in the macrophages of the spleen, is so outstanding in this disease that hemolysis in its more exact sense is to be questioned, at least as the main mechanism of erythrocyte destruction in the newborn infant. In addition to the specific destructive effect of antibodies on the Rh-positive erythrocytes, sensitizing antibodies may also play an important and devastating role. Although "sensitization" is a concept frequently employed by investigators in this field, it has not been made clear what factor produces this sensitization, or whether other tissues than the erythrocytes are directly involved. Analysis of our cases has led us to conclude that anti-Rh globulin may cause diverse effects, and that one of these effects may be sensitization of the anaphylactic type.

In case 1, for example, the damage to liver and lungs resulting in the hemorrhagic diathesis, as well as the erythroblastemia, is more adequately explained on the basis of passive sensitization than by anemia or "hemolysis." Neither the erythrocyte level nor the decreasing jaundice suggests sufficient reason for the definite injury to the liver. Yet injury to this organ undoubtedly was responsible for the widespread hemorrhages. Our observations, moreover, indicate that even severe anemia, when uncomplicated by other factors, is not accompanied by erythroblastemia. A considerable increase in nucleated red blood cells

10. Koucky, R. W.: Experiences with the Rh Substance in Transfusion Reactions, Minnesota Med. **26**:980 (Nov.) 1943.

11. Wiener, A. S.: A New Test (Blocking Test) for Rh Sensitization, Proc. Soc. Exper. Biol. & Med. **56**:173 (June) 1944.

12. Race, R. R.: An Incomplete Antibody in Human Serum, Nature, London **153**:771 (June 24) 1944.

13. Wiener, A. S.: Conglutination Test for Rh Sensitization, J. Lab. & Clin. Med. **30**:662 (Aug.) 1945; Rh Factors in Clinical Medicine, ibid. **30**:957 (Nov.) 1945; Pathogenesis of Congenital Hemolytic Disease (Erythroblastosis Fetalis): I. Theoretic Considerations, Am. J. Dis. Child. **71**:14 (Jan.) 1946.

14. Abt, A. F.: Anemia of the Newborn, Am. J. Dis. Child. **43**:337 (Feb.) 1932. Sennott, J. S.: Erythrophagocytosis in Acute Hemolytic Anemia of the Newborn: A Report of Three Cases, ibid. **71**:269 (March) 1946.

in the peripheral circulation, however, is produced in dogs by anaphylactic shock, presumably due to the anoxic anoxemia resulting from the reaction.[15] This suggests anaphylaxis as a mechanism for the erythroblastemia and associated erythroblastosis. The erythroblastemia is thus unrelated to the red cell level, as we have found, yet represents a compensatory effort on the part of the organism, which is correlated with changes in the lungs and the liver of the affected child. Evidence of hepatic injury, on the other hand, is absent in babies with the aregenerative form of congenital anemia, although the anemia, resulting from rapid destruction of erythrocytes, may become extremely severe. With such destruction of erythrocytes, why does not the "cellular debris" accumulating in the "end capillaries" [2] cause damage comparable to that which it is presumed to cause in icterus gravis neonatorum and fetal hydrops? Clinical study indicates that it does not; such study suggests, however, that the symptoms and signs which differentiate the erythroblastic from the nonicteric, aregenerative form (and phase) of "hemolytic disease of the newborn" are the symptoms and signs produced by sensitization.

These symptoms are found to a remarkable degree in case 1. In this baby sensitizing antibodies as well as isoagglutinins[16] appear to have been transmitted not only through the placenta but also through the mother's milk. The increased permeability of the capillaries, with extravasation of blood into stomach and bowel, the increased fluidity of the blood and the edema, hemorrhages and cellular proliferation in the lungs are consistent with repeated and protracted anaphylaxis.[17] The histologic changes in the liver, too, are similar to those seen following anaphylaxis both in man[18] and in dogs.[19] Longcope,[20] fur-

15. Dean, H. R., and Webb, R. A.: The Blood Changes in Anaphylactic Shock in the Dog, J. Path. & Bact. **27**:65 (Jan.) 1924.

16. Witebsky, E.; Anderson, G. W., and Heide, A.: Demonstration of Rh Antibody in Breast Milk, Proc. Soc. Exper. Biol. & Med. **49**:179 (Feb.) 1942. Witebsky, E., and Heide, A.: Further Investigations on Presence of Rh Antibodies in Breast Milk, ibid. **52**:280 (April) 1943.

17. While our data do not include platelet studies, Sanford has pointed out that platelets are decreased in erythroblastosis fetalis,[40] an effect which likewise is consistent with anaphylaxis (Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice: A University of Toronto Text in Applied Physiology, ed. 3, London, Baillière, Tindall & Cox, 1943).

18. Dean, H. R.: The Histology of a Case of Anaphylactic Shock Occurring in a Man, J. Path. & Bact. **25**:305 (July) 1922. Ziskind, J., and Schattenberg, H. J.: Fatal Anaphylactic Shock in Man, Arch. Int. Med. **62**:813 (Nov.) 1938. Werne, J., and Garrow, I.: Fatal Anaphylactic Shock: Occurrence in Identical Twins Following Second Injection of Diphtheria Toxoid and Pertussis Antigen, J. A. M. A. **131**:730 (June 29) 1946.

(Footnotes continued on next page)

thermore, has called attention to the slight cirrhosis in the liver which results from repeated sublethal anaphylactic reactions. Repeated reactions due to sensitizing antibodies transferred through the milk thus offer a complete and cogent explanation for the symptoms and organic changes found in this case.

The mechanism by which the anaphylactic reaction produces these injurious changes has long been of intense interest to immunologists. Dragstedt and Gebauer-Fuelnegg [21] have shown that the lymph and the blood collected from the liver of the dog during anaphylactic shock contains a substance identical with or closely resembling histamine in its physicochemical properties and pharmacologic effects. These studies corroborate the conclusions of Dale,[22] who has pointed out that "in the dog the specific anaphylactic sensitization by antibody chiefly affects the liver cells. . . . When these are injured, by the immune reaction occurring in their protoplasm, histamine which we know them to contain, is released in such quantities as to produce its effects not only on the liver vessels but on the histamine sensitive cells of the body at large. . . . The cell injury, however, is not limited to the degree required to produce a release of histamine, and involves other and more direct results." These other results have been discussed by Feldberg,[23] who states that "the 'injury' may involve, in addition, processes which result in the formation from the tissue constituents of toxic substances, the effects of which may participate even in immediate anaphylactic manifestations. The resemblance between anaphylactic and peptone shock . . . is more complete than that between anaphylactic and histamine shock. . . . The coagulability of the blood is lost . . . due to the liberation from the liver of an anticoagulant substance which is probably identical with heparin." Thus the anaphylactic response produces an intoxication, as indicated by the experiments of Manwaring

19. Dean, H. R., and Webb, R. A.: The Morbid Anatomy and Histology of Anaphylaxis in the Dog, J. Path. & Bact. **27**:51 (Jan.) 1924.

20. Longcope, W. T.: Cirrhosis of the Liver Produced by Chronic Protein Intoxication, Tr. A. Am. Physicians **28**:497, 1913.

21. Dragstedt, C. A., and Gebauer-Fuelnegg, E.: Studies in Anaphylaxis: Appearance of Physiologically Active Substance During Anaphylactic Shock, Am. J. Physiol. **102**:512 (Nov.) 1932. Gebauer-Fuelnegg, E., and Dragstedt, C. A.: Studies in Anaphylaxis: Nature of Physiologically Active Substance Appearing During Anaphylactic Shock, ibid. **102**:520 (Nov.) 1932.

22. Dale, H. H.: Croonian Lectures on Some Chemical Factors in the Control of the Circulation, Lancet **1**:1233 (June 15); 1285 (June 22) 1929.

23. Feldberg, W.: Histamine and Anaphylaxis, in Luck, J. M., and Hall, V. E.: Annual Review of Physiology, Stanford University, Calif., Annual Reviews, Inc., 1941, vol. 3, p. 671.

and his group.[24] The anaphylatoxin, however, is no longer a hypothetic abstraction, but a group of identifiable chemical substances released from the sensitized cell on the union of antigen with specifically modified globulin within the cell protoplasm. Such toxic substances are the result, not the cause, of the anaphylactic reaction, but once released they bring about their damaging effects on susceptible tissues throughout the organism.

In the human being as in the dog the liver is a "shock organ," although it shares this susceptibility with other tissues, notably the lungs. In the Rh-positive fetus of an Rh-negative sensitized mother the liver would be particularly vulnerable. Not only is it the organ through which antibody-bearing blood direct from the placenta first flows, but lining the sinusoids are the Kupffer cells, which are actively engaged in the disintegration of erythrocytes containing the Rh antigen. On release of this antigen it is free to be absorbed by the adjacent hepatic cells. That this actually occurs is indicated by the experiments of Boorman and Dodd,[25] who utilized the principle of "specific inhibition" to show that the Rh factor is present in hepatic cells, lymph nodes, spleen and other organs. The reaction which may ensue, as sensitizing antibodies unite with the Rh antigen within the hepatic cells, would then result in the release of substances having an adverse effect on many parts of the body. The antigen-antibody reaction may take place in other cells than those of the liver, however. Lungs, brain—even the placenta—might in some cases suffer profoundly from this reaction, as well as from intoxication by substances produced by reacting cells elsewhere in the fetal or infant organism.

Evidence suggesting that sensitization of tissue may occur in other organs in this disease is found in case 12. In this case the anti-Rh globulin seems to have been directed only slightly against the erythrocytes. It was definitely productive of organic injury, however, the brain being outstandingly affected. The cause of this injury to the brain is debatable. Certainly anemia was not a factor, and while the icterus index on the seventh day was 180, this value is not so high as that found at the end of the first day of life in case 6, in which the brain was unaffected. This is hardly compatible with the concept that there is a significant causal relationship between the degree of bilirubinemia and nuclear jaundice. Moreover, the pigment in the brain and the tissues of babies

24. Manwaring, W. H.; Hosepian, V. M.; O'Neill, F. I., and Bing Moy, H.: Hepatic Reactions in Anaphylaxis; X. The Hepatic Anaphylatoxin, J. Immunol. **10**:575 (May) 1925; The Hepatic Anaphylatoxin Studied by Hepatic Transplantation and Blood Transfusion, J. A. M. A. **83**:2092 (Dec. 27) 1924.

25. Boorman, K. E., and Dodd, B. E.: The Group-Specific Substances A, B, M, N and Rh: Their Occurrence in Tissues and Body Fluids, J. Path. & Bact. **55**:329 (July) 1943.

with nuclear icterus differs from that found on necropsy in jaundiced infants not so affected, as pointed out long ago by Schmorl.[26] Anoxia, however, may have been severer in our case than the clinical picture suggested. Intoxication must also be considered. In addition, there remains the possibility that during fetal life sensitizing antibodies direct from the placenta might in part have evaded retention within the hepatic cells; by traversing a patent ductus venosus and foramen ovale they might then have been carried upward to the brain, there sensitizing the cells of the nuclear areas. The specific reaction with Rh antigen (or hapten) within the sensitized cells would then produce cellular changes which, unlike injury in other organs, would be irreversible.

Case 12, as has been noted, is remarkable for the slight degree of destructive effect on the red cells during the first days of life. It seems as if the Rh-positive erythrocyte-destroying antibodies were here conspicuous by their absence, at least until the mother's milk provided a further supply. This is in sharp contrast to the destruction of erythrocytes produced by the immune reaction in cases 2 and 11. This divergence from the usual course suggests the independent action in this disease of two apparently distinct antibodies, the erythrocyte-destroying factor and a sensitizing antibody which conceivably reacts with the Rh antigen or hapten. In most instances the effects of these two antibodies would seem to run parallel. There are instances, however, as in case 12, in which one type of antibody action seems to predominate significantly over the other.

The pathologic and clinical evidence in our cases strongly suggests this mechanism of a dual antibody action. The erythrocyte-destroying antibodies may be represented as causing changes within the Rh-positive erythrocytes which intensify manyfold their destruction by phagocytosis within the body. The sensitizing antibodies, on the other hand, show themselves clinically in the symptoms of intoxication and in jaundice, edema, anoxia, erythroblastemia, the hemorrhagic diathesis and spasticity denoting injury to the brain. On the basis of such a mechanism, differences in the severity of the manifestations and in the complications of erythroblastosis fetalis would depend on (*a*) the degree of sensitization, (*b*) the tissues sensitized, (*c*) the number of erythrocyte-destroying antibodies gaining entrance into the child's body, and (*d*) the response of the individual child. Only a small amount of sensitizing globulin would be sufficient to produce deleterious effects, depending on the organ or organs involved. If the placenta is affected by the allergic reaction or by one or more anaphylatoxic substances, the child might die in utero from asphyxia or miscarriage might occur. If the vascular endothelium

26. Schmorl, G.: Zur Kenntnis des Ikterus neonatorum, insbesondere der dabei auftretenden Gehirnveränderungen, Verhandl. d. deutsch. path. Gesellsch. **6**:109, 1903.

is the "shock organ" [27] fetal hydrops might be the result, the placenta sharing in the edema that would develop. If the brain is sensitized, irreparable injury would be done to the central nervous system, although the child might suffer less from intoxication than when the liver is primarily concerned. If the liver is the organ predominantly sensitized, jaundice and the intoxication produced not only by the anaphylactic reaction but also by the metabolic and other effects of damage to the liver would produce a severe icterus gravis which would nevertheless be amenable to treatment resulting in complete recovery without residual effects. The reason for the greater frequency of the icterus gravis type of the disease is apparent, since the liver would in most cases be effective in filtering out the sensitizing antibodies. Finally, if the sensitizing antibodies were minimal or lacking and the erythrocyte-destroying antibodies predominated, the condition resulting would be that represented clinically by congenital anemia.

If it is assumed that these two antibodies may each produce effects independently, it seems probable that both a state of sensitization and a state of immunity may exist together in babies with erythroblastosis fetalis. This is indicated by the sharp difference in the clinical condition before and after treatment noted in cases 2 and 11. Following birth the symptoms of intoxication dominated the picture, although the progressive anemia revealed the isoimmune process. After treatment had ameliorated these symptoms, presumably achieving a desensitization, the immune reaction involving the red cells continued. The "immune" state in these infants was then clearly differentiated from the previous condition assumed to be complicated by hypersensitivity. Rich, Jennings and Downing [28] have shown that in the case of bacterial allergy sensitization and immunity can both exist as simultaneous states in the same animal. While intracutaneous sensitization caused extensive inflammation with pronounced necrosis of the tissue at the site of injection, the immunity reaction protected the animal from an otherwise lethal dose of the antigenic bacteria. After desensitization by intravenous administration of the killed bacteria, however, the immunity was unimpaired, but the antigen-antibody reaction produced only a minute and insignificant necrotic lesion.

As in bacterial allergy, a clearcut distinction between the hypersensitive state and the immune condition can be noted in our cases. The condition of the individual affected infant, according to this view, is thus a resultant of these two independent variables. While these two

27. Moon, V. H.: The Pathology and Mechanism of Anaphylaxis, Ann. Int. Med. **12**:205 (Aug.) 1938.

28. Rich, A. R.; Jennings, F. B., Jr., and Downing, L. M.: The Persistence of Immunity After the Abolition of Allergy by Desensitization, Bull. Johns Hopkins Hosp. **53**:172 (Oct.) 1933.

states are both based on antigen-antibody relationships, immunity connotes a condition essentially benign, while sensitization may give rise to injury. Hypersensitivity, however, is susceptible of modification, and this is usually accomplished by the proper administration of additional antigen. It is thus not necessary that "repeated stimulation" and the increased formation of antibodies assumed to take place in the Rh-negative mother with each succeeding pregnancy produce manifestations of increasing severity of the disease in successive offspring. This is often not the case. Actually an increasing titer of isoagglutinins in the mother during pregnancy has not infrequently been associated with unexpectedly mild symptoms in the child. This is unexplained if isoagglutinins are responsible for the severe manifestations of the disease in the child. If, however, they represent an "immune" response, a minimal effect on the child can be understood. Furthermore, something like a partial desensitization appears to have occurred spontaneously in an occasional baby in a series with familial erythroblastosis fetalis; for while the clinical sequences of the disease in successive affected children of the same mother are usually remarkably similar, an increased severity in a later child is noted no more often than a decreased severity. I. A. Abt [29] reported the case of an infant with familial jaundice of the newborn that recovered spontaneously after several siblings had died of icterus gravis with hemorrhagic manifestations. Abbott and Abbott [30] presented the case of a baby with aregenerative congenital anemia who recovered uneventfully after the first child of the parents had died on the third day of icterus gravis with erythroblastosis, the second on the fifth day of congenital anemia with leukoblastosis and the third pregnancy had resulted in a spontaneous abortion. Burnham,[31] Dockeray and Sachs,[32] Mollison,[33] and Henry [34] have each reported normal children with Rh-positive blood born by mothers with Rh-negative blood, whose serum contained demonstrable anti-Rh agglutinins. Davidsohn stated that "the order is not necessarily from the least severe form (anemia) to the

29. Abt, I. A.: Familial Icterus of New Born Infants, Am. J. Dis. Child. **13:** 231 (March) 1917.

30. Abbott, K. H., and Abbott, F. F.: Idiopathic Anemia of the New Born: Review of Literature and Report of Two Cases, Am. J. Dis. Child. **49:**724 (March) 1935.

31. Burnham, L.: The Common Etiology of Erythroblastosis and Transfusion Accidents in Pregnancy, Am. J. Obst. & Gynec. **42:**389 (Sept.) 1941.

32. Dockeray, G. C., and Sachs, H.: Rh Antibodies in the Maternal Circulation Without Clinical Manifestations of Erythroblastosis in the Child, J. Immunol. **48:**241 (April) 1944.

33. Mollison, P. L.: The Application of Present Knowledge About the Rh Factor, Post-Grad. M. J. **20:**17 (Jan.) 1944.

34. Henry, N. R.: Rh Factor and Prognosis, M. J. Australia **2:**114 (July 29) 1944.

most severe (hydrops)."[35] The patient in case 11, presented here, was the fourth child, following 2 stillborn infants the description of whom suggests intrauterine or intrapartum death from fetal hydrops. Thus it appears not only that the titer of isoagglutinins in the mother's serum is not an index of the degree of sensitization in the child, a fact now generally recognized, but also that the degree of passive sensitization may sometimes be favorably modified in a later child.

The concept of anaphylactic sensitization in this disease[36] provided the basis for a plan of treatment, first used in 1937 (case 2), designed to combat this sensitization and to limit or remedy the resulting hepatic injury.[37] The treatment included intravenous transfusions of compatible blood, a therapy already used successfully by others for some years. After Levine's discovery of the role of the Rh factor it seemed to us that Rh-positive blood should achieve desensitization more effectively than Rh-negative blood. In view of the stress that has been and is currently being placed on the use of Rh-negative blood, in the treatment of erythroblastosis fetalis, presumably to avoid a destructive reaction between the Rh-positive cells of the donor and the antibodies derived from the mother, it may be well to examine briefly the immunologic mechanisms involved.

In the baby with Rh-positive blood the only anti-Rh globulin molecules are derived solely from the sensitized mother. They are maximal at birth, diminishing as they are absorbed by the Rh-positive cells or Rh antigen of the infant.[38] Additional Rh-positive cells transfused into the Rh-positive baby, therefore, will be vulnerable to the action of the anti-Rh erythrocyte-destroying antibodies, but they can actually cause no "increased hemolysis." Destruction of erythrocytes in the baby is a function of maternal antibody action alone. Only additional specific antibodies from the mother's blood or milk can increase the amount of destruction of Rh-positive cells within the baby's body. In the baby whose own blood possesses the antigen, therefore, there is no "transfusion reaction" effect on administration of Rh-positive blood, such as occurs in the sensitized mother whose antibodies are unabsorbed.

With the antibody content of the infant's body thus limited, prompt desensitization would seem to be advisable. Slowing this process by

35. Davidsohn, I.: Fetal Erythroblastosis, J. A. M. A. **127**:633 (March 17) 1945.

36. Darrow, R. R.: Icterus Gravis (Erythroblastosis) Neonatorum: An Examination of Etiologic Considerations, Arch. Path. **25**:378 (March) 1938.

37. Darrow, R. R.: The Treatment of Erythroblastosis Fetalis, J. A. M. A. **127**:1146 (April 28) 1945.

38. Danis, P. G.; Eto, J. K., and Sennott, J. S.: The Use of Rh Positive Blood Cells in the Treatment of Erythroblastosis Fetalis, J. Pediat. **28**:457 (April) 1946.

permitting radical depletion of the Rh-positive cell content of the infant's body is the currently recommended procedure, however. In those cases in which sensitization is moderate and in which the isoimmune reaction produces considerable destruction of erythrocytes predominantly, the nonspecific desensitization provided by the administration of Rh-negative blood may be adequate. That in some instances it is not is indicated by the occasional unexpected death of an affected infant whose erythrocyte count has been kept at a high level with Rh-negative blood. With Rh-positive blood, on the other hand, the symptoms of intoxication decreased after the first transfusion and were never noted after the second. Of the 3 babies who received only Rh-positive blood, none showed jaundice for more than fifteen days. The rapid disappearance of the symptoms of intoxication and the speedy clearance of the jaundice suggest significant improvement in hepatic function. Such effects, assumed to be attributable to specific desensitization, would seem to be of at least equal importance with the maintenance of a normal level of red cells and hemoglobin. That Rh-negative blood in the treatment of erythroblastosis fetalis is superior in both of these respects has yet to be demonstrated.

While the use of Rh-positive blood in these cases has been entirely justified by the results obtained, the response to plasma was unexpected and disappointing. Since erythrocytes did not seem to be required in case 6, at least during the first twenty-four hours, it was thought that plasma should have a desirable diluting effect on any intoxicating factors, preserve the level of the plasma proteins and combat other "shock" effects. A protective action, however, could not be demonstrated. Its administration was ineffective compared with that of blood. It thus appears that the effectiveness of blood transfusion in this disease may be ascribed principally to the cells, even in those cases in which the erythrocyte level is still relatively high and in which oxygen is being given at least intermittently. In case 2, for example, the edema, lethargy and nervous hyperirritability were dramatically relieved, albeit temporarily, by the first transfusion, and did not reappear after the second, while the progress of the baby receiving plasma continued steadily downhill, reaching after two transfusions of plasma a state of considerable intoxication before the first transfusion of Rh-positive blood was given. The transfused blood given in this case, it may be noted, was of the same Rh type as that of the blood of the infant's father.

Our experience with the exclusive use of Rh-positive blood in the 3 cases presented here, as well as in 2 subsequent cases, corroborates that of others. Burnham, for example, gave three transfusions of father's blood to an infant presenting pronounced anemia, jaundice, erythroblastemia and petechiae, with complete recovery of the infant.[31]

Koucky,[10] Turner,[39] Sanford[40] and Danis, Eto and Sennott[38] have likewise each found that Rh-positive blood may be used with entire success. Father's blood in some cases has seemed to be particularly effective,[41] possibly because its desensitizing action is enhanced by its specificity.

The pathologic processes affecting both the erythrocytes and the liver in the icterus gravis form of the disease are operating before birth, as they are in those cases in which the babies are stillborn or hydropic. Considerable anemia and a positive direct van den Bergh reaction have both been noted in the cord blood. In spite of this, none of these babies were icteric and they all seemed quite vigorous at birth. Within a few hours, however, the picture changed precipitately. Birth seems to be a significant factor in the extremely rapid downhill course. Explanation may be based on two assumptions: (1) that in utero the mother's circulation carries off the products of excess destruction of fetal red cells, together with toxic substances generated in the fetal organism, the mechanism suggested by Palm,[42] and (2) that the uterine contractions ending in birth, either normal or by cesarian section, are responsible for an increased or a new influx of antibodies from the maternal into the fetal circulation. This has been suggested by Wiener for the bivalent (agglutinating) antibodies[43] and would seem to be even more true for the sensitizing factors. These antibodies would thus have their chief effects in the period immediately following birth, and damage to liver and lungs resulting from the sensitization reaction would accelerate the deterioration. If these assumptions are valid, premature delivery is not indicated. Prompt treatment after delivery, however, is of the utmost importance.

CONCLUSIONS AND SUMMARY

Analysis of observed cases of erythroblastosis fetalis not only corroborates Levine's theory of isoimmunization but supports also the concept of sensitization of the anaphylactic type. These two states, both based on antigen-antibody relationships, appear to be present to varying extents in the affected child but are not necessarily parallel in occurrence

39. Turner, O. E.: Investigation of Transfusion Reactions, Pennsylvania M. J. **47**:1071 (Aug.) 1944.

40. Sanford, H. N.: Jaundice in the Newborn, M. Clin. North America **30**:75 (Jan.) 1946.

41. Danis, Eto and Sennott.[38] Frankowski, C., and Darrow, R. R.: Treatment of Passive Rh Isosensitization in the Newborn (Erythroblastosis Fetalis) with Rh Positive Blood: Use of Blood of the Same Rh Type as That of the Father, J. Am. M. Women's A. **1**:207 (Oct.) 1946.

42. Palm, H.: Zur Frage der Entstehung des Kernikterus der Neugeborenen, Monatschr. f. Geburtsh. u. Gynäk. **49**:264, 1919.

43. Wiener, A. S.: Notes on the Pathogenesis of Congenital Hemolytic Disease (Erythroblastosis Fetalis), Am. J. Clin. Path. **16**:319 (May) 1946.

or severity. This produces the extreme variety and complexity of symptoms which have seemed so confusing.

The passive isoimmune reaction is presumed to take place between the specifically modified (maternal) globulin and the baby's Rh-positive erythrocytes, resulting in their destruction. The reversed, passive isosensitization reaction, on the other hand, would be expected to occur within the tissue cells, principally those of the liver, between the specific sensitizing antibody and the Rh antigen freed by the destruction of the Rh-positive erythrocytes. This intracellular reaction produces injury to the cell, causing histamine and other cellular constituents having toxic effects to be released into the circulation. These substances, in turn, have a damaging effect on susceptible tissues elsewhere in the body. The increased bilirubin produced by the destruction of Rh-positive erythrocytes intensifies the jaundice caused by the hepatic inadequacy due to the sensitization reaction. A hemorrhagic diathesis would be the result of severe, prolonged or repeated injury to the liver caused by the sensitization reaction within the hepatic cells. Proteins in the blood would tend to be lowered, both because the damaged liver could not form them and because the increased permeability of the capillaries would permit their escape from the vascular system. Edema would be the result of such loss, more especially if the endothelium were directly sensitized. Histamine produced by reacting sensitized cells in liver or lungs or both would cause edema of the pulmonary alveolar walls, this in turn resulting in an anoxic anoxemia. The same reaction affecting the placenta could produce intrauterine death from asphyxia. Injury to the brain, resulting in nuclear icterus, could be due to anoxia, to intoxication or to direct sensitization of the nuclear neurons, the affected cells showing a greater avidity for circulating pigment than the surrounding brain tissue. That bilirubinemia resulting from destruction of erythrocytes can produce selective injury to the brain is open to question.

The rapid deterioration of affected babies after birth may be explained as due both to the loss of the protective function of the maternal circulation and to an augmented influx of specific, maternal antibody globulin with the uterine contractions incidental to evacuation of the uterus.

Rh-positive blood was used exclusively in 3 of the cases reviewed. The results were entirely favorable; this was presumably due in part to the desensitizing action of the transfused cells, as well as to their oxygen-carrying function.

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PATHOGENESIS OF MONGOLISM

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THE PATHOLOGIC evidence presented in this paper tests a hypothesis that whatever the cause of mongolism may be [1] the condition originates between the sixth and the ninth week of fetal life. This evidence is based on the established features of the disorder supplemented by observations from the protocols of fifty autopsies performed during the past twenty-five years at the Children's Hospital in Boston.

The pathology of mongolism has been extensively studied by Brousseau and Brainerd,[1a] Benda [1b] and many others.[2] These investigations show no anatomic system to escape from at least occasional anomalous development.

ESTABLISHED ANATOMIC FEATURES

Skull.—Bullard [2g] studied roentgenograms of 25 mongoloid skulls thirty-five years ago and concluded that "the cranium is not only so

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1. (*a*) Brousseau, K.: Mongolism: Study of Physical and Mental Characteristics of Mongolian Imbeciles, revised by H. G. Brainerd, Baltimore, Williams & Wilkins Company, 1928. (*b*) Benda, C. E.: Mongolism and Cretinism: The Interaction of Endocrine Glands, New York, Grune & Stratton, Inc., 1946. (*c*) Ingalls, T. H.: The Etiology of Mongolism, to be published.

2. (*a*) Macklin, M. T.: Am. J. M. Sc. **178**:315, 1929. (*b*) Ford, N., and Frumkin, S.: Monozygosity in Mongoloid Twins, Am. J. Dis. Child. **63**:847 (May) 1942. (*c*) Hill, W. B.: Quart. J. Med. **2**:49, 1908-1909. (*d*) Brushfield, T.: Brit. J. Child. Dis. **21**:241, 1924. (*e*) Comby, J.: Arch. de méd. d. enf. **20**:505, 1917; (*f*) ibid. **30**:5, 1927. (*g*) Bullard, W. M.: Boston M. & S. J. **164**:56, 1911. (*h*) Benda, C. E.: Am. J. Path. **16**:71, 1940. (*i*) Clift, M. W.: Am. J. Roentgenol. **9**:420, 1922. (*j*) Muir, J., abstracted, Arch. Pediat. **20**:161, 1903. (*k*) Jansen, M.: Feebleness of Growth and Congenital Dwarfism with Special Reference to Dysostosis Cleido-Cranialis, London, Oxford University Press, 1921, p. 51. (*l*) Ormond, A. W.: Tr. Ophth. Soc. U. Kingdom **32**:69, 1911. (*m*) van der Scheer, W. M.: Beitrage zur Kenntnis der mongoloiden Missbildung (Mongolismus), Berlin, S. Karger, 1927; cited by Davidoff.[2o] (*n*) Gans, A., cited by Davidoff.[2o] (*o*) Davidoff, L. M.: Brain in Mongolian Idiocy: Report of Ten Cases, Arch. Neurol. & Psychiat. **20**:1229 (Dec.) 1928. (*p*) Hefke, H. W.: Roentgenologic Study of Anomalies of Hands in One Hundred Cases of Mongolism, Am. J. Dis. Child. **60**:1319 (Dec.) 1940.

small as to be technically microcephalic, but is brachycephalic, i.e., the transverse diameter is excessively large in proportion to the shortened anteroposterior diameter. It immediately suggests that this condition may have some relation to the shape or size of certain bones at the base of the cranium." Even before the advent of the roentgen ray, there was agreement on this feature which Benda has recently reemphasized in commenting on the lack of proliferation and regularity in "the cartilaginous bones [i.e., derived from cartilage] at the base of the skull." [2h]

Facies and Nose.—The facies was described by Brousseau and Brainerd [1a] as "flattened and broad . . . often depressed due to the short, squat nose with its shrunken bridge." The cartilaginous part is wide, often flaring and triangular, and the nostrils face forward rather than downward. Brushfield [2d] noted a squat nose in 50 per cent and a broad nose in 26 per cent of 173 patients.

Nasal Bones, Maxilla and Palate.—In a roentgenologic study of 55 skulls, Clift [2i] found without exception that the "acral parts of the nose and maxilla are poorly developed." He concluded that the mongoloid skull is characterized by acromicria, the term being used "in opposition to acromegaly in which we find the most extreme development of these parts." Greig [3] in a craniometric study of 3 skulls found both nasal bones congenitally lacking in the first, the left nasal bone lacking in the second and both nasal bones present, though dwarfed, in the third. Muir [2j] noted a high palate in 10 (37 per cent) of 26 mongoloid patients. The deficiency of the maxilla is accompanied by a real, or more probably an apparent, largeness of the tongue, and not infrequently by relative prognathism.

The Eye.—The eye has a narrow palpebral fissure, usually slanting upward and outward. An epicanthal fold was evident in 39 per cent of Brushfield's patients.[2d] Jansen [2k] ascribed the orbital slant to dwarfism of the nasal bones. Ormond [2l] reported some form of opacity of the lenses in half of his 42 cases, varying from a single opaque dotlike mass to a completely formed lamellar cataract. Strabismus is not uncommon and occasionally develops after birth.[2j]

The Ear.—The ears are small, badly developed and generally asymmetric.[2d] They may be malplaced, the lobule may be small, atrophied or absent, and Darwinian tubercles are occasionally noted. They are frequently chimpanzee-like.[1a]

The Brain.—Van der Scheer [2m] found the average weight of the brain for 18 mongoloid children to be low, judged by the age of the patients. The brain tended to be spherical with a short anteroposterior and a wide lateral diameter. The medulla and the pons were strikingly

3. Greig, D. M.: Edinburgh M. J. **34**:253, 1927.

small in comparison with the rest of the brain. Dwarfism of the midbrain, especially in the region of the interpeduncular space, was a characteristic of 6 brains.

Studying the same material, Gans [2n] found 1 brain with a depression instead of the normal elevation of the olive together with a dwarfing of the cerebellum on the opposite side; in another, the accessory olives were small. Davidoff [2o] also found relatively narrow anteroposterior and wide lateral diameters in the 10 brains he studied, and agreed with van der Scheer that this was "altogether due to the almost constant brachycephaly." Among other constant morphologic changes, the small size of the cerebellum and the brain stem, an embryonic convolutional pattern and a paucity of ganglion cells in the third cortical layer were listed. These changes were interpreted to represent (1) agenesis as evidenced by poverty of cells and failure of gyral development, (2) aplasia as shown by the small size in comparison with normal brains of corresponding age and (3) paragenesis as demonstrated by the frequent occurrence of anomalies.

Skeleton.—The short, fat, stumpy hands and feet are outstandingly characteristic of the mongol. Bullard found that roentgenograms of the long bones revealed "chiefly differences in size and stage of development between these patients and normal persons of the same age." The retardation in growth is particularly noticeable in the metacarpals and the phalanges, and anomalous formation of the second phalanx of the fifth finger was demonstrated roentgenologically by Hefke[2p] in 62 per cent of 100 cases. Brousseau and Brainerd reported 8 instances of syndactyly of the toes and stated that syndactyly of the fingers has been noted by Comby and Kiellner.[1a] Sutherland [4] described a right hand with short thumb and incurved little finger, while the left hand showed shortening of the thumb and a complete webbing of the third, fourth and fifth fingers.

The Heart and the Blood Vessels.—Numerous observers have stressed the association of congenital cardiac anomalies and mongolism.[5] On clinical evidence, the correlation is usually placed around 20 per cent,[1a] though the figure is higher for cases studied pathologically.[2c,d] Abbott [6] has stressed as a "feature of extraordinary interest . . . the frequent combination of mongolian idiocy with the persistent ostium primum.[7] This combination calls for explanation."

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4. Sutherland, G. A.: Practitioner **63**:632, 1899.

5. Brousseau.[1a] Hill.[2c] Brushfield.[2d] Comby.[2e]

6. Abbott, M. E.: Atlas of Congenital Cardiac Disease, New York, American Heart Association, 1936, p. 50.

7. "A failure of upward growth of the ventricular septum combined with an arrest of fusion of the auriculo-ventricular cushions with the free lower border of the septum primum." [6]

Various deformities of the valves and the great vessels are relatively common, including persistent ductus arteriosus, pulmonary stenosis and aortic stenosis.

Endocrine Glands.—There is general agreement that the genitalia, particularly in males, are clinically underdeveloped after infancy and that normal sexual maturity is rarely if ever attained.[1ab] That such lack of sexual development might bear a relation to hypoplasia of the adrenal cortex (in turn secondary to the primary cause of mongolism) is the opinion of Hirning and Farber.[8] They made measurements of the adrenal glands of 15 mongoloid persons and compared the results with measurements on a series of suitable controls. No characteristic pathologic changes were found during the first year of life, but with advancing maturity increased evidence of a definite hypoplasia of the permanent cortex was noted.

In exceptional instances anomalies of the other endocrine glands are found. Thus absent thymus, persistent thymus, pituitary dwarfism, pituitary enlargement and absence of the thyroid gland have each been reported on occasion.[1a] As a generality however, Brousseau and Brainerd concluded that "there are no constant pathologic lesions of the ductless glands such as are found in cretinism." In sharp contrast, Benda [1b] has concluded that there is a constant pathologic condition of the pituitary gland as evidenced by deficiencies or abnormalities of intracellular secretory granules. "Mongolism is the congenital type of hypopituitarism."

Miscellaneous.—Brousseau and Brainerd stressed as an outstanding feature of mongolism the great variety of lesions to be found, with no one peculiar to the condition. While the cranial stigmas are essential to recognition, they listed no less than eighty-six commonly associated anomalies and functional disorders. The majority, such as ectropion, blepharitis, myotonia and hydrocephalus, cannot be said to have their origin at any particular stage of fetal development. Those susceptible of orientation in embryonic life are narrow, oblique palpebral fissures, malformed ears, smallness of the nasopharynx, slit nostrils, a defective and abnormally high palate, defects of the interventricular septum, spina bifida, syndactyly of the fingers, syndactyly of the toes, small, undeveloped and undescended testicles, hypospadias and atresia ani.

OBSERVATIONS AT AUTOPSY

The following observations, for the most part macroscopic, are presented compositely. It appears irrelevant to include available histologic minutiae when the purpose of this study is to determine general patterns and to interpret their significance. A composite of deformities

8. Hirning, L. C., and Farber, S.: Am. J. Path. **10**:435, 1934.

is not difficult to construct, although variations are both numerous and bizarre, some occurring frequently and others in a small fraction of the series.

Skull and Facies.—The established cranial and facial characteristics were invariably present. Indeed, they are essential for diagnosis. Excerpts from typical records read "the configuration of the skull is striking on account of the small size of the frontal bones compared to the parietal" and "there is upward and outward slanting of the palpebral fissures, a flattened glabellum, and a tongue which protrudes approximately 5 mm. beyond the gum margins."

In 1 infant (age 1 day), the shape of the ears was "striking due to angulations of the upper part of the external margin," i. e., darwinian tubercles. In a second (age 1 month), the ears had a "thin cartilaginous skeleton . . . with an extra fold beneath the crux of the helix bringing the external auditory canal somewhat below its usual position and concealed behind the lobe." A left "preauricular appendage" was noted in a third (age 3 months). Pronounced micrognathia was seen once.

The Brain.—In only 2 of 13 cases did the weight of the brain surpass the normal for the age of the patient. One infant died of intrauterine asphyxia (weight of brain, 400 Gm.; normal for age, 335 Gm.), and the other (age 2 months) (weight of brain, 790 Gm.; normal for age, 715 Gm.) died of left-sided cardiac decompensation. Both showed evidence of cerebral edema. The average weight of the brain for the other 11 was 81 per cent of the expected normal. The general observations of van der Scheer, Gans and Davidoff were confirmed. Individual anomalies were present in 3 of the 13 cases. One infant (age 5 months) had on the under surface of the cerebellum "a depression on the right, just posterior to the tonsil" about 3 by 2 mm. in diameter. In another (age 3 months), there was "blurring and indistinctness of the markings of the pons and medulla." The vessels of the brain also showed anomalous development. The circle of Willis was "somewhat abnormal on the left . . . and . . . the left posterior cerebral artery was smaller than that on the right. The left posterior communicating artery was very small and situated further laterally than that on the right." This patient also had "fan-shaped" venous formations in the cerebrum. The most striking malformation was that of an infant (age 1½ months) with marked hypoplasia of the cerebellum, pons and medulla (fig. 1). Sections of the brain showed a "small cartilaginous oval glistening mass, 0.5 by 0.35 cm., located just posterior to the hypophyseal stalk." It was thought to be a suprasellar tumor.

Skeleton.—The well known characteristics of the mongoloid hand and foot, like those of the facies, were observed so regularly as merely

to confirm previous observations. A typical description reads "digits are short and tapering. The fifth fingers are relatively shorter—not, however, curved inward." In other instances, the curved fifth finger was observed. Variations were not infrequent. In 1 child (age 12 years), the little finger was observed to be "proportionately longer and thinner than the remaining digits—and curved medially." In another infant (age 2 months), there was bilateral webbing of the second and third toes.

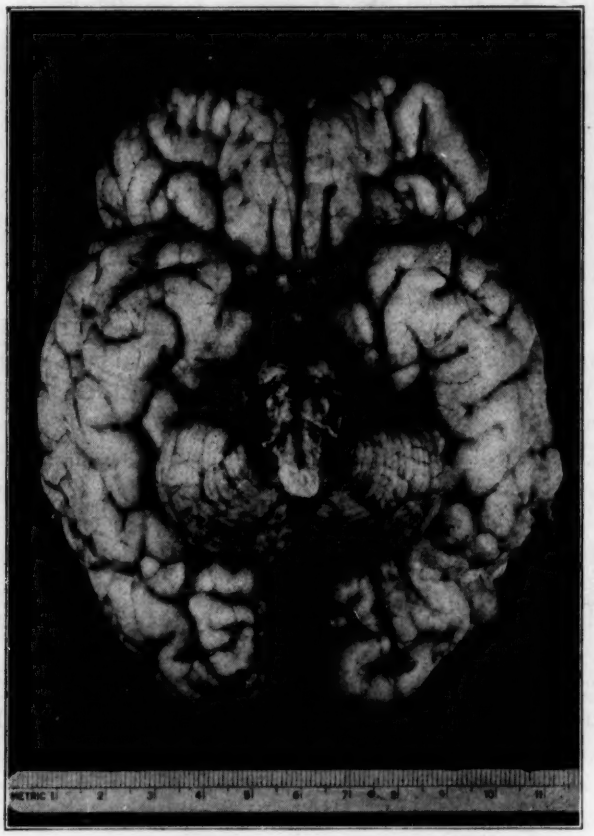

Fig. 1.—Brain of a mongoloid infant 1½ months of age illustrating hypoplasia of the cerebellum, the pons and the medulla.

The most striking variation was a "congenital malformation of the right foot more consistent with an aplastic process than with a uterine amputation." The right foot "consists only of the os calcis and talus. The skin is stretched over these bones and there are two toe nails laterally corresponding to the little toe and the one next to it, and a rudimentary toe nail a short distance medially." Photographs and roentgenograms of this child (age 18 months) are shown in figure 2.

The Heart and the Blood Vessels.—An interauricular defect (persistent ostium primum) was found in the heart of 8 of 32 persons. Fourteen others had interventricular defects, making a total 22 of 30 mongoloid children with demonstrable septal defects. In general, when septal defects were present the heart was globular and valvular insufficiency was frequently manifest. Thus, 2 infants (ages 26 days and

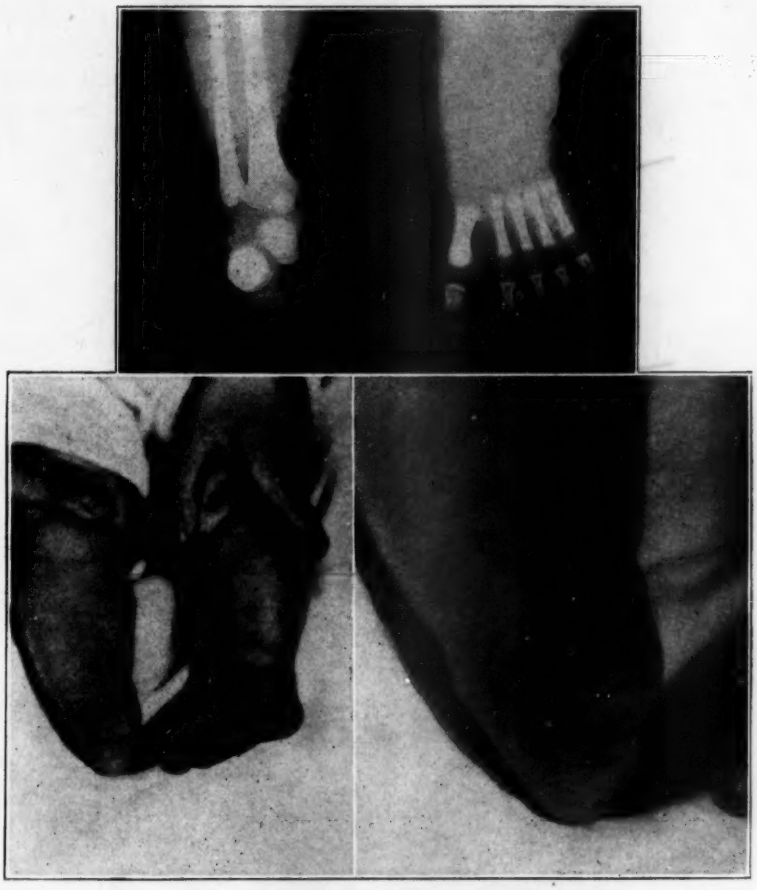

Fig. 2.—Roentgenograms and photographs of lower extremities of a mongoloid infant 18 months of age. In the right foot rudimentary toe nails may be distinguished in the photograph while the roentgenogram reveals complete aplasia of the metatarsal bones and phalanges. It may be seen that the distal phalanges of the left foot are rudimentary and the middle row is dwarfed—except for the great toe.

8 months) were observed to have both mitral and tricuspid insufficiency; another (age 48 months), a complete division of the tricuspid valve (fig. 3), while a fourth (age 16 months) had a bifid conformation of the anterior mitral cusp, together with a patent ductus arteriosus, hypoplasia of the aorta and hyperplasia of the pulmonary artery. A

persistent left superior cava entering the right atrium via a coronary sinus and a retroesophageal right subclavian artery were associated with the septal defect of 1 infant (age 1 month).

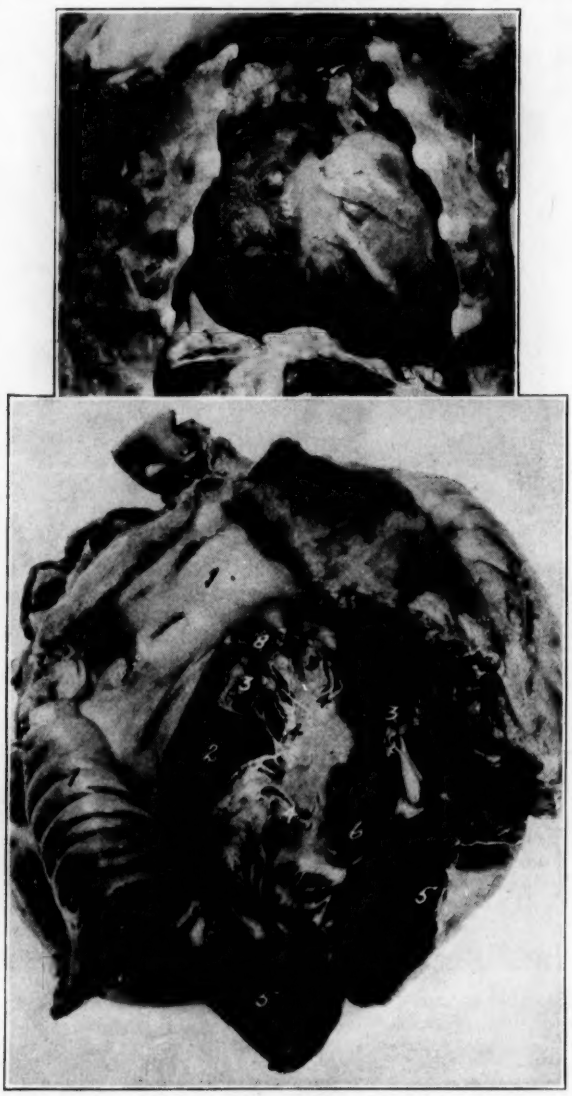

Fig. 3.—Heart showing (1) right auricle; (2) persistent ostium primum; (3) tricuspid valve, with one cusp bifid; (4) anomalous chordae tendinae; (5) wall of right ventricle; (6) right ventricle; (7) mitral valve and, (8) fusion of mitral and tricuspid valves. Note the globular contour of the unopened heart and the vertical position of the auricular-ventricular septum.

Two babies (ages 1½ months and 3 months, respectively) had a patent ductus arteriosus in addition to septal defects, the first with an

associated dextroposition of the aorta, and the second with anomalous origins of branches arising from the aortic arch. One infant (age 3 months) had a septal defect and dextroposition of the aorta, while the ductus passed to the left and formed an arterial ring around the trachea and esophagus.

Various anomalies of systemic arteries and veins were frequent The patient with multiple anomalies of the cerebral circulation has already been mentioned, as have those who showed anomalous branchings arising from the aorta. Two other infants had aberrant vessels to the left kidney. In one (age 5 weeks), the kidney was "J shaped," and the infant also had pyloric stenosis. An anomalous left innominate vein and left hepatic vein were found in a baby 2 months of age.

Endocrine Glands.—No characteristic gross or microscopic pathologic conditions of the endocrine glands were determined for patients of this series. In the large majority of cases all endocrine glands were grossly normal, though the infants were so young for the most part that the gross appearance of the gonads was not informative. Both the sella turcica and the pituitary gland were found in 1 instance to be unequivocally small, and an instance of suprasellar tumor has been referred to previously. One infant (age 26 days), dying from cardiac decompensation, in addition to multiple cardiac defects had "very few intact acini" in the thyroid gland, the significance of which could not be evaluated, and another lacked demonstrable thymus tissue. Acidophilic cells not infrequently predominated in the pituitary gland, although at other times a predominance of basophilic cells was noted. However, serial sections of the glands were not made, and consequently estimates are not given of the distribution of chromophilic cells in the hypophysis.

The adrenal glands of 15 of the patients have been the object of histologic study by Hirning and Farber,[8] as has been previously noted.

Miscellaneous.—Two infants, curiously enough, died of leukemia, 1 (age 8 weeks) of acute myelogenous leukemia, and the other (age 19 months) of acute lymphatic leukemia.[9]

In addition to typical mongoloid stigmas, 4 babies had malattachment or malrotation of the mesentery. There were one instance of "J-shaped kidney" and one of pyloric stenosis.

COMMENT

Retarded and Anomalous Development of the Skull and the Brain.—The essence of the cranial abnormalities has been demonstrated to reside in moderate microcephaly, definite brachycephaly and relative dwarfism

9. This observation is passed with the single comment that if any association exists between mongolism and leukemia it would appear to hold more import for students of the latter than of the former subject.

of the basilar bones and the contiguous glabellum, the nasal bones and the maxilla. The cerebral abnormalities consist principally of a relatively narrow anteroposterior and a wide lateral diameter of the brain, the organ conforming to the general shape of the skull; relative dwarfing of the cerebrum, the cerebellum and the brain stem, and not infrequently anomalous formations which vary among the persons examined.

These pathologic conditions unquestionably have their origin well before birth and long before death. The active process being unavailable for study, the abnormalities observed must be viewed as late manifestations. From them, attempt may be made to reconstruct the sequence of past events. As long ago as 1899, Sutherland [4] suggested that the altered shape of the skull might depend on either (1) premature ossification of the basilar bones or (2) defective growth in the structures at the base of the brain. He could find no evidence indicative of premature

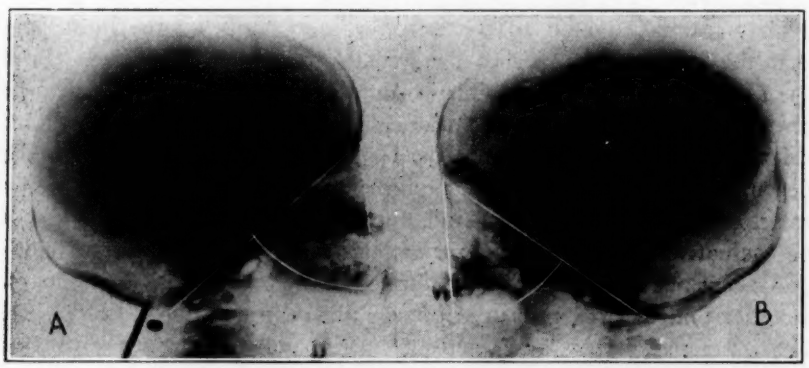

Fig. 4.—*A*, a normal skull; the hiatus between the sphenoid and occipital bones representing the spheno-occipital cartilage may be seen. *B*, a mongoloid skull; dwarfing of the acral parts, representing lack of forward development of the face and the basilar part of the cranium, may be seen. In this particular instance the nasal bones are absent. When present, they will constantly be found to be dwarfed.

synostosis and therefore concluded that the relative agenesis of the basilar encephalon resulted in a comparable deformity of the skull. By 1928, Brousseau and Brainerd could justifiably pronounce that the theory of premature synostosis had been "abandoned."

Some of the extensive work during the past few decades [10] on growth of bone now makes apparent that premature synostosis is not the only mechanism by which cranial growth may be interrupted. If one substitutes "retarded development" for "premature ossification," Sutherland's first hypothesis cannot be easily abandoned.

10. (*a*) Wolbach, S. B.: Proc. Inst. Med. Chicago **16**:118, 1946. (*b*) Benda.[2b] (*c*) Ingalls, T. H.: Endocrinology **29**:710, 1941. (*d*) Stoccada, F.: Beitr. z. path. Anat. u. z. allg. Path. **61**:450, 1916; cited by Benda.[1b]

In order to explore this hypothesis anew, attention is desirably focused on the spheno-occipital cartilage. Closely behind the sella turcica the sphenoid terminates in a cartilaginous plate which separates it from the occipital bone. Stoccada [10d] has described the normal development of this structure and the alterations which occur in cretinism. Benda [2h] has called attention to its lack of development in mongolism and Greig [3] to an instance of its premature synostosis in mongolism. Sufficient emphasis has not been accorded to the fact that the spheno-occipital plate has all the histologic and roentgenologic characteristics of an epiphysis, even that of closure when growth has been completed. There is much to support the concept that the spheno-occipital cartilage is an epiphyseal mechanism by which the greater increment of forward growth of the base of the skull is accomplished.

If this interpretation of function be correct, then normal development of the spheno-occipital epiphysis would be expected to be impeded by the same general deficiencies of hormones and vitamins [10e] or by other disease processes [11] which retard epiphyseal growth elsewhere. The end result would be brachycephaly and also microcephaly unless there is also a compensatory enlargement of the vault as in achondroplasia. Brachycephaly is manifested clinically by the depressed glabellum of syphilis and cretinism. The depressed glabellum is common to these otherwise unrelated conditions, as it is to mongolism and to achondroplasia, in which incapacity of the cartilage to grow to average length appears to be inherited.[12] In animals, this characteristic follows mendelian laws, and purebred strains have been developed in many species, such as Dexter Kerry cattle, Ancon sheep and the English bulldog.[13] The dachshund appears to represent a breed with chondrodystrophic cartilage of the epiphyses of the limbs but not of the skull. The boxer, originally a cross between the English bulldog and a mastiff, has a chondrodystrophic skull but well developed limbs.

Cranial and cerebral growth keep pace with each other so precisely that gross disturbances of the one organ may well affect the other. Although it has long been recognized that agenesis of the brain may result in microcephaly, the reciprocal proposition has only recently been established experimentally. Wolbach and Bessey [14] showed that the lesions of nervous tissue from animals on diets deficient in vitamin A are wholly of mechanical origin and due to a disproportionately slow

11. The case of the infant with the small cartilaginous tumor "just posterior to the hypophyseal stalk" is of interest in view of these considerations. The proximity to the spheno-occipital plate is so great as to suggest that the tumor may have originated from it.

12. Porter, J. H.: Brit. M. J. **1**:12, 1907.

13. Landauer, W.: Sigma Xi Quart. **28**:171, 1941.

14. Wolbach, S. B., and Bessey, O. A.: Vitamin A Deficiency and Nervous System, Arch. Path. **32**:689 (Nov.) 1941.

growth of the cranium in relation to the brain. This results in overcrowding of the cranial cavity, distortion of the brain and herniation of its contents. A similar phenomenon does not necessarily occur in mongolism, but the possibility warrants investigation. Such an investigation would desirably correlate both clinical and pathologic findings with cranial deformities. For example, the strabismus so frequently observed in mongolism could originate from bony compression of the sixth nerve as it courses along the base of the skull. Such fine correlations are not made in the course of ordinary necropsies, although Grieg [8] found numerous asymmetries in the cranial floors of the 3 mongoloid skulls which he examined. In 1 skull the "large development of the tuberculum sellae obscured the sulcus chiasmaticis to some extent."

The observation of morphologic deformities in the pons, the medulla and the cerebellum of patients with mongolism was provocative, though sufficiently detailed descriptions of the floor of the skull were not available in this series for comparison of the cranium with its contents. Morphologically, the inner surface of the skull may be looked on as an impression of the brain, or the brain may be regarded as a cast of the skull. Future careful comparison of adjacent contours may indicate an interrelated pathologic process. It is probable that before such a comparison could be made, the brain should be fixed in situ, as was done by Wolbach [10a] in his later work on vitamin A deficiency as it affected the brain.

That the genesis of the cerebral abnormalities may yet be found to reside primarily or concomitantly in cerebral damage or anomalous vascular supply should not be overlooked. To date, however, neuropathologists have not elicited evidence of a primary insult within the brain. Davidoff, on the basis of his own work and that of predecessors in the field, could not have committed himself more strongly than when he attributed the general contours of the mongolian brain "altogether to the almost constant brachycephaly."

Time of Origin of the Anomalies.—The multiplicity and nature of the deformities that were found in this series of necropsies give weight to a concept that mongolism arises from damage to embryonic tissue.

Ordinarily the stigmas are not sufficiently evident for the condition to be recognized in the premature stillborn fetus.[15] It is of interest, therefore, that the youngest infant in this series was a premature baby 40 cm. in length and weighing 3 pounds 6 ounces (1,476.9 Gm.). There are many reasons for believing that the observed anomalies originate before the third month of gestation. Such gross abnormalities as septal defects, transposition of great vessels, aberrant vessels and fusions of digits must have their origin at an early stage of pregnancy. Many

15. Hertig, A.: Personal communication to the author.

observers have been convinced that the causative influences operate so early as to antedate the formation of the blastoderm.[16] Much of the case on which such a conclusion is based derives from the frequency with which mongolism occurs in homozygous twins as compared with heterozygous twins. The subject will not be discussed at length. It will suffice to comment here that if the preembryonic milieu is identical for each of homozygous twins, the early embryonic milieu must be nearly so. The point to be emphasized is that a greater frequency of mongolism among homozygotes as contrasted with heterozygotes would not of itself suffice to prove that the condition arose in the ovum or sperm rather than in the early embryonic period.

It seems fair to say that, on the basis of available facts, the time of origin may be narrowed down to a period lying between preembryonic and early embryonic life (probably before the third month) of the affected person. The time cannot be ascertained precisely without further embryologic study.[1c] However, Weatherford [17] is of the opinion that each of the anomalous conditions susceptible of orientation in embryonic life [18] represents an arrested or disturbed gradient of growth during the sixth to ninth week of gestation. If it could be proved that the time of origin of the skeletal, cardiac, vascular and other anomalies centers at this stage of pregnancy, it would tend to orient the sequence of events which results in the loose symptom complex of mongolism.

Essential Nature of the Anomalies.—Mongolism is generally regarded as a more or less uniform syndrome, and occasionally as a primary endocrine disorder.[1b] It is difficult, however, to connect darwinian tubercles, congenital cataracts, polydactyly, septal defects, dextroposition of the aorta and malattachment of the mesentery with any known endocrine dysfunction. There would appear to be no more compelling reason to explain the whole syndrome in terms of endocrine abnormality than in terms of cranial or cardiac abnormality. If, in the words of Maude Abbott, the combination of mongolian idiocy with persistent ostium primum "calls for explanation," so, too, do the combinations with syndactyly, cleft palate and atresia ani. The almost constant association with anomalies of early vascular development suggests that many anatomically unrelated defects may have a common denominator in endothelial abnormality. The frequent association of aplasia of the acral parts and the dwarfed middle phalanx of the fifth finger with syndactyly, polydactyly and other skeletal defects suggests that developing masses of precartilage and membranous centers of ossification

16. (*a*) Southwick, W. E.: Time and Stage in Development at Which Factors Operate to Produce Mongolism, Am. J. Dis. Child. **57**:67 (Jan.) 1939. Macklin.[2a] (b) Russell, P. M. G.: Lancet **1**:802, 1933.

17. Weatherford, H. L.: Personal communication to the author.

18. These anomalous conditions are listed under "Miscellaneous," p. 282.

throughout the skeleton may be affected by the etiologic agent in chance combinations and that the involvement of the tribasilar bone may simply be one of them—the essential one for the production of the cranial stigmas. Each anomaly may be merely a member of a larger group subject to numerous permutations and combinations—the result of an etiologic agent, not the cause of a syndrome. If this is so, 100 cases of mongolism, like 100 cases of persistent ostium primum or syndactyly, are all parts of a larger biologic phenomenon—like bulbar and spinal paralysis, which are only parts of the total manifestation of poliomyelitis.

The investigative eye should then be directed to scrutiny of the events occurring at the time when the anomalies come into being. The recent discovery that maternal rubella may result in such widely separated sequelae in the fetus as congenital cataracts, anomalies of the heart, brachycephaly and mental retardation [19] warrants a fresh appraisal of congenital anomalies in general, and mongolism in particular, in relation to maternal illness.[20] There is evidence that many pregnancies which result in the delivery of a mongoloid infant are abnormal in important respects.[21]

SUMMARY

Mongolism is interpreted as a variable syndrome made up of specific anomalies subject to numerous permutations. The final combination always includes brachycephaly and dwarfism of the basilar portion of the skull, the pathogenesis of which is discussed. The association of cranial with numerous skeletal anomalies suggests that developing masses of precartilage and membranous centers of ossification throughout the skeleton are affected in chance combinations. The involvement of the tribasilar bone may simply be one of them—the essential one for the production of the cranial stigmas, but of no etiologic significance.

It is suggested that attention be centered on the sixth to ninth weeks of fetal life in the search for possible etiologic agents. This is the period when the anomalies susceptible of embryologic orientation appear to arise.[1c]

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19. Gregg, N. M.: M. J. Australia **1**:313, 1945. Swan, C.; Tostevin, A. L.; Moore, B., and Black, G. H. B.: ibid. **1**:409, 1944.

20. Aycock, W. L., and Ingalls, T. H.: Am. J. M. Sc., to be published.

21. Ingalls, T. H., and Davies, J. A. V.: New England J. Med., to be published. Footnote 1.

BLOOD PRESSURE OF NORMAL GIRLS FROM THREE TO SIXTEEN YEARS OF AGE

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THE PRESENT study of blood pressure was begun at the Child Research Council in Denver. Much of the literature was covered at that time and initial experiments concerning blood pressure were carried out. The data for the study have been gathered from girls at the University of Chicago Laboratory School.

REVIEW OF LITERATURE

The first to measure blood pressure was Stephen Hales, in England, who in 1733 attached a glass tube 12 feet and 9 inches (389 cm.) long to the left carotid artery of a horse, held the tube vertically and found the blood to rise to a height of 9 feet and 6 inches (290 cm.).[1] Poiseuille introduced the U form of mercury manometer in 1828.[2] Von Basch[3] was the first to perfect a sphygmomanometer for clinical use. His had a glass cylinder containing a rubber bulb connected with a mercury manometer, later with a spring manometer. The open end of the glass cylinder was covered with a membrane. The cylinder was filled with water and was called a pelotte. The membrane of the pelotte was pressed over an artery against a bone. Potain's sphygmomanometer, 1889, replaced the water by air.[2] Riva-Rocci in 1896 introduced the manometer of which most of the modern types are modifications.[4]

There has always been a question as to the effect on the blood pressure reading of the amount of soft tissue of the arm and the width of the cuff. In 1900 Gumprecht[5] expressed the opinion that the soft tissue absorbed part of the pressure of the cuff so that the true arterial pressure is lower than that registered by the manometer. He did experiments which consisted of taking blood pressure with a Riva-Rocci cuff

1. Carlson, A. J., and Johnson, V.: The Machinery of the Body, ed. 2, Chicago, University of Chicago Press, 1941, p. 180.

2. Janeway, T. C.: The Clinical Study of Blood Pressure, New York, D. Appleton and Company, 1907.

3. von Basch, S.: Measurement of Blood Pressure in Human Beings, Ztschr. f. klin. Med. **2**:79, 1880.

4. Frohlich, E.: Two Hundred Years of Blood Pressure Measuring, München. med. Wchnschr. **80**:1479 (Sept. 22) 1933.

5. Gumprecht: Experimental and Clinical Tests with the Riva-Rocci Sphygmomanometer, Ztschr. f. klin. Med. **39**:382, 1900.

(which is 4.5 cm. wide [6]) and at the same time measuring the pressure directly, and found pressures 40 to 60 points higher with the cuff. Von Recklinghausen [7] stated the belief that it was not the soft tissue around the artery which caused the readings to be too high but a too narrow cuff. He explained this by using the analogy of blocks collapsing a rubber tube. A single block must be heavier to cause compression of the tube than the individual blocks in a row since the single one must alone overcome the resistance to the deformed position and compress the tube. In a row of blocks only the end ones must hold the tube in the deformed position. He stated the belief that if cuffs of two widths

TABLE 1.—*Blood Pressure in Millimeters*

Authors	Kaupe [11] 1910		Judson and Nicholson [14] 1914		Nirrnheim [15] 1916	Faber and James [16] 1921		Burlage [17] 1922	
Size of cuff	Wide		9 cm., 3-7 yr. 13 cm., 8-15 yr.		12 cm.	7.5 cm., 10 cm., 12.5 cm.		12 cm.	
Method	Palpatory		Auscultatory		Palpatory and oscillatory	Auscultatory		Auscultatory	
Type of apparatus	Riva-Rocci		Modified Erlanger		von Reckling-hausen	Mercury manometer		Mercury manometer	
Years	Boys	Girls	Systolic	Diastolic	Systolic	Boys	Girls	Sys-tolic	Dias-tolic
3	77/70	78 - 108/75 - 96	92	58	.....	89/60	88/59	...	..
4	81 - 98/73 - 87	81 - 90/74 - 81	92	61	.....	89/60	88/59	...	..
5	.....	78 - 88/68 - 81	91	60	.....	92/62	90/62	...	..
6	88 - 96/79 - 87	79 - 98/70 - 90	93	63	75.7 - 95.6	94/64	93/64	...	..
7	91 - 98/82 - 95	83 - 117/75 - 105	87	64	79.4 - 94.1	97/65	97/66	...	..
8	97/85	72 - 110/66 - 101	93	59	81.6 - 97	99/66	100/67	...	..
9	89/80	80 - 100/72 - 91	91	62	83.8 - 113.2	100/67	101/69	104	68
10	103/95	87 - 102/79 - 94	99	64	81.6 - 108.6	102/68	102/70	108	65
11	96/87	90 - 106/81 - 100	95	62	85.3 - 111.7	104/69	104/71	109	64
12	.....	79 - 100/69 - 92	99	59	89.7 - 112.5	105/71	106/71	114	68
13	98.5/88.5	89 - 111/81 - 102	104	68	94.8 - 127.2	107/71	108/73	118	71
14	.....	.....	105	63	94.1 - 113.2	110/73	109/73	123	76
15	.....	.....	99	61	.....	112/74	112/76	123	73
16	.....	.....	..	..	.....	115/75	114/79	118	73
17	.....	.....	..	..	.....	.....	.....	115	75
18	.....	.....	..	..	.....	.....	.....	111	74
19	.....	.....	..	..	.....	.....	.....	111	73
20	.....	.....	..	..	.....	.....	.....	109	74

are used, one on one arm and one on the other, and the narrow cuff gives the same reading as the wide, the narrow one is still wide enough to be correct, but if it gives a higher reading, it is too narrow. Sainsbury [8] expressed the opinion that the pulse disappears when the cuff pressure is raised, not because the artery is compressed, but because the extravascular pressure cancels the expanding force of the pulse wave and the blood stream becomes a steady, not a pulsating one.

6. Schilling, T.: Blood Pressure Measurements, München. med. Wchnschr. **53**:1105 (June 5) 1906.

7. von Recklinghausen, H.: Blood Pressure Measuring in Humans, Arch. f. exper. Path. u. Pharmakol. **46**:78, 1901.

8. Sainsbury, H.: State of the Artery and the Circulation Under the Sphygmomanometer Cuff During Compression, Brit. M. J. **1**:191 (Feb. 2) 1929.

Sahli concluded that a wider cuff absorbs too much of the impulse of the pulse wave so that the radial pulse is obliterated before the pressure in the cuff has reached the true intra-arterial pressure.[6] Schilling [6] determined blood pressure with cuffs 14 cm., 11.2 cm. and 8 cm. wide and found differences of 7 to 17 mm. of mercury between the widest and narrowest. He also compared the readings by direct and indirect methods on the thigh of a calf and found that an 8 cm. cuff gives almost the same pressure as the direct method, but that a 12 cm. cuff gives a reading which is too low. He found higher readings when an arm was wrapped with gauze bandage to increase its circumference, but

of Mercury According to Age in Years

Lincoln [18] 1928		Sundal [20] 1929		Chabrun and Petrovitch [21] 1930		Richey [22] 1931		Bogdanovitch [23] 1934	
9.5 cm.		12 cm.		12 cm. 12-15 yr. 5 cm. 4-12 yr.		12 cm.		12 cm. 11-15 yr. 5 cm. 5-11 yr.	
Auscultatory		Palpatory		Auscultatory		Auscultatory		Auscultatory	
.....		von Recklinghausen Modification of Riva-Rocci		Vaquez-Laubry		Baumanometer		Vaquez-Laubry	
Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
93/66	89/67	75.8	77.5	.....	.....	.....	.....	.....	.....
94/67	93/66	82.3	80.0	100.0/77.5	97.9/79.5	.....	.....	101/70	99/71
98/70	95/67	80.9	81.5	103.2/80.7	101.7/83.4	80/49	84/57	104/74	102/75
98/70	97/69	86.5	84.1	103.8/87.3	104.8/87.2	85/52	85/56	105/79	106/79
98/70	99/70	88.3	86.0	106.0/87.7	107.2/80.0	88/55	89/57	110/80	109/77
100/73	100/71	90.2	90.2	109.7/89.7	110.0/88.0	92/57	92/59	111/82	112/81
101/72	101/71	91.0	86.2	111.5/87.5	104.8/83.0	94/60	92/59	113/80	107/76
105/75	104/74	90.7	97.1	108.0/83.0	110.0/83.8	95/60	96/61	110/76	112/77
104/73	105/74	98.5	102.4	106.0/72.0	111.6/88.0	96/62	100/64	109/72	117/81
102/73	104/75	104.6	105.7	120.0/95.0	116.0/93.0	98/61	102/64	122/87	118/85
105/75	105/74	108.5	109.0	114.0/87.0	121.0/85.0	100/62	103/65	116/83	123/82
.....	.....	111.4	109.1	120.0/100.0	122.0/86.5	106/64	103/67	122/95	124/83
.....	.....	111.5	108.5	114.0/88.0	119.5/87.7	110/66	105/67	117/84	122/84
.....	.....	115.1	108.5	.....	.....	111/66	106/69	.....	.....
.....	.....	112.8	106.9	.....	.....	111/67	102/66	.....	.....
.....	.....	114.1	109.1	.....	.....	112/68	100/66	.....	.....
.....	.....	115.6	110.7	.....	.....	117/68	104/66	.....	.....
.....	.....	113.0	114.0	.....	.....	.....	.....	.....	.....

Masson [9] found a negligible increase when a pad of fat was wrapped around the arm to increase its circumference.

In his work with blood pressures in well children, Eminet [10] tested children who lived under relatively good, medium and poor conditions. He found the blood pressure higher in the first group. He found two peaks in the blood pressure curve, one at about 6 years and one at 11 years. Kaupe [11] used a Riva-Rocci apparatus with a wide sail cloth cuff.

9. Masson, C. B.: Influence of Soft Parts on Blood Pressure, M. J. & Rec. (supp.) **122**:210 (Aug. 19) 1925.

10. Eminet, P. P.: Sphygmography and Tonometry in Well Children 7-15 Years of Age, Arch. f. Kinderh. **46**:328, 1907.

11. Kaupe, W.: Blood Pressure in Childhood, Monatschr. f. Kinderh. **9**:257, 1910.

He expressed the opinion that the systolic pressure is the point at which the radial pulse disappears. He found higher pressures in stronger children, little variation with sex and increased blood pressure with fear or anxiety over the procedure. Wolfensohn-Kriss [12] carried out her research using both a Riva-Rocci and a Sahli modification of

TABLE 2.—*Blood Pressure in Millimeters of Mercury According to Weight in Kilograms*

Authors	Wolfensohn-Kriss [12] 1910		Michael [13] 1911	Nirrnheim [15] 1916	Burlage [17] 1923		Sundal [20] 1929	
Size of cuff	6 cm.		9 cm.		12 cm.		12 cm.	
Method	Palpatory		Palpatory	Palpatory and oscillatory	Auscultatory		Palpatory	
Type of apparatus	Riva-Rocci		Cook's Modification of Riva-Rocci	von Recklinghausen	Mercury manometer		von Recklinghausen Modification of Riva-Rocci	
Weight in Kg. (Pounds in Parentheses)	Systolic	Diastolic			Systolic	Diastolic	Boys	Girls
12.5 - 15 (27.5 - 33)			95				76	77
15 - 17.5 (33 - 38.5)	65 - 100	60 - 95		75.7 - 94.1			80	81
17.5 - 20 (38.5 - 44)			100		80	57	84	83
20 - 22.5 (44 - 49.5)	80 - 110	75 - 100		77.2 - 113.2			87	85
22.5 - 25 (49.5 - 55)			107		104	61	90	92
25 - 27.5 (55 - 60.5)	85 - 115	75 - 100		81.6 - 105.1			93	95
27.5 - 30 (60.5 - 66)			112		104	63	96	103
30 - 32.5 (66 - 71.5)	80 - 120	75 - 110		83 - 111.7			100	103
32.5 - 35 (71.5 - 77)			116		108	66	106	105
35 - 37.5 (77 - 82.5)	80 - 115	75 - 110		94.1 - 119.1			107	107
37.5 - 40 (82.5 - 88)			122		113	69	108	109
40 - 42.5 (88 - 93.5)	90 - 125	85 - 115	126	101.4 - 127.2	116	70	110	108
42.5 - 45 (93.5 - 99)							110	107
45 - 50 (99 - 110)	95 - 130	90 - 120			114	73	112	110
50 - 55 (110 - 121)	90 - 140	80 - 130			113	73	112	108
55 - 60 (121 - 132)					113	74	115	111
60 - 65 (132 - 143)					114	75	114	104
65 - 70 (143 - 154)					114	77	116	106
70 - 75 (154 - 165)					124	82	115	
75 - 80 (165 - 176)					123	80	128	

von Basch's apparatus. With the Riva-Rocci apparatus a cuff 6 cm. wide was used. The van Basch apparatus was easier to use on infants. The systolic pressure was taken as the point at which the radial pulse disappeared. She used well children 2 to 17 years old and found the

12. Wolfensohn-Kriss, P.: On the Blood Pressure in Childhood, Arch. f. Kinderh. **53**:332, 1910.

blood pressure to increase with age, with height and with weight. In the same age group but with different height or different weight, the blood pressure was different. There was no variation with sex. Michael [13] tested the blood pressures in 128 normal children. She found that, though the blood pressure seems to increase with increasing age, height and weight, if one divides the blood pressure by the surface area of the arm compressed, the blood pressure will be found to remain rather constant.

TABLE 3.—*Blood Pressure in Millimeters of Mercury According to Height in Centimeters*

Authors	Oppenheimer and Bauchwitz* 1905	Michael [13] 1911	Nirrnheim [15] 1916	Burlage [17] 1923		Sundal [20] 1929	
Size of cuff	5 cm.	9 cm.		12 cm.		12 cm.	
Method	Palpatory	Palpatory	Palpatory and oscillatory	Auscultatory		Palpatory	
Type of apparatus	Sahli modification of Riva-Rocci	Cook's modification of Riva-Rocci	von Recklinghausen	Mercury manometer		von Recklinghausen modification of Riva-Rocci	
Height in Cm. (Inches in Parentheses)				Systolic	Diastolic	Boys	Girls
50 (19.6)	82	...	.....	..	..	..	..
60 (23.6)	85	...	.....	..	..	..	..
70 (27.5)	102	...	.....	..	..	..	..
80 (31.5)	94	...	.....	..	..	..	..
90 (35.4)	110	...	.....	..	..	74	72
95 (37.4)	...	...	.....	..	..	79	81
100 (39.3)	92	...	75.7 - 81.6	..	..	79	81
105 (41.3)	...	99	79.4 - 83.4	..	..	82	80
110 (43.3)	109	...	77.2 - 94.1	84	63	86	88
112.5 (44.25)	...	...	.....	..	..	..	..
115 (45.2)	...	...	82.7 - 105.1	..	..	87	84
117.5 (46.25)	...	...	.....	72	50	..	..
120 (47.2)	115	109	79.4 - 113.2	98	66	88	89
122.5 (48.2)	...	...	.....	102	66	..	..
125 (49.2)	...	...	81.6 - 104.3	104	64	91	89
130 (51.2)	...	112	85.3 - 110.2	104	61	91	93
135 (53.1)	...	118	83 - 119.1	107	62	96	102
140 (55.1)	...	120	89.7 - 113.2	110	65	103	104
150 (59)	...	125	107.4 - 111.7	113	70	109	107
160 (63)	...	...	.....	114	76	114	111
170 (66.9)	...	...	.....	116	78	115	108

* Arch. f. Kinderh. 42 : 415.

Judson and Nicholson [14] stated their belief that the width of the cuff should be proportionate to the circumference of the arm. In children from 4 to 8 years old the 9 cm. cuff gave results as accurate as those with the wider cuff. They found a slight but gradual rise in systolic pressure from 3 to 10 years and a more abrupt rise from 10 to 14 years. Nirrnheim [15] had 5 boys and 5 girls in each age group. He used both

13. Michael, M.: A Study of Blood Pressure in Normal Children, Am. J. Dis. Child. **1**:272 (April) 1911.

14. Judson, C. F., and Nicholson, P.: Blood Pressure in Normal Children, Am. J. Dis. Child. **8**:257 (Oct.) 1914.

15. Nirrnheim, E.: The Normal Blood Pressure in Childhood, Monatschr. f. Kinderh. **13**:20, 1916.

TABLE 4.—*Longitudinal Recordings for Individual Girls (Ten Year Follow-Up)*

Subject	Age	Weight, Pounds	Height, Inches	Percentage: Over Average Weight	Percentage: Under Average Weight	Blood Pressure Reading: Child Cuff	Blood Pressure Reading: Adult Cuff
C. A.	5 yr. 11 mo.	45.25	44.29	5	....	80/50	
	6 yr. 11 mo.	50	46.45	3.4	....	90.54	
	7 yr. 11 mo.	58.5	48.74	7.9	....	.....	80/56
	8 yr. 9 mo.	67	50.66	12.2	....	.....	96/60
	9 yr. 9 mo.	74.5	53.26	8.7	....	.....	96/56
	10 yr. 11 mo.	84.25	56.33	6.2	....	.....	98/64
	11 yr. 9 mo.	93.25	58.85	4.3	....	.....	92/62
	12 yr. 11 mo.	104.25	60.9	3	....	.....	106/70
	13 yr. 10 mo.	110.75	61.7	2.8	....	122/58	106/68
	15 yr. 1 mo.	109	62.2	...	4	110/70	100/62
C. B.	4 yr. 9 mo.	37.25	41.73	0	0	84/56	
	5 yr. 10 mo.	39.75	43.85	....	5.2	84/60	
	6 yr. 8 mo.	44.5	45.9	....	1.5	96/54	
	7 yr. 8 mo.	48.5	47.79	....	5.9	.....	86/64
	8 yr. 8 mo.	52.5	50.15	....	9.8	.....	96/58
	9 yr. 8 mo.	57.5	51.41	....	7.6	.....	98/58
	10 yr. 10 mo.	62	53.38	....	10.3	.....	96/64
	11 yr. 9 mo.	66.25	54.76	....	10.4	.....	104/68
	12 yr. 9 mo.	71.75	56.5	....	11.4	.....	98/68
	14 yr.	85	60.4	....	17.1	114/78	96/74
C. C.	5 yr.	50.75	46.45	5.8	....	100/62	
	6 yr. 1 mo.	60.75	49.88	9	....	98/68	
	7 yr.	67.25	52.06	6.3	....	.....	102/64
	8 yr.	76	55.03	5.5	....	.....	102/70
	9 yr.	84.25	57.67	3.5	....	.....	106/66
	10 yr.	95.75	60.03	5.2	....	.....	88/52
	10 yr. 11 mo.	102.25	61.89	....	1.1	.....	92/64
	11 yr. 11 mo.	111.5	63.89	....	1.1	.....	100/68
	13 yr. 1 mo.	119.5	66	....	3.7	106/78	96/64
	14 yr. 4 mo.	127.5	67	....	2.5	104/66	90/72
C. D.	4 yr. 2 mo.	42	41.92	8	....	82/58	
	5 yr. 3 mo.	48.75	44.68	10.6	....	86/54	
	6 yr. 4 mo.	64.25	47.95	23.7	....	86/68	
	7 yr. 4 mo.	79.75	51.06	34.4	....	.....	96/68
	8 yr. 2 mo.	87.75	53.26	29.8	....	.....	98/54
	9 yr. 2 mo.	94	56.77	19	....	.....	104/64
	10 yr. 2 mo.	108	59.56	21	....	.....	90/58
	11 yr. 2 mo.	124.5	62.48	17	....	.....	96/56
	12 yr. 4 mo.	149.75	64	31	....	.....	108/74
	13 yr. 6 mo.	159.5	64	37.4	....	110/80	94/72
A. U.	5 yr.	45.0	45.47	0	0	92/68	
	6 yr. 2 mo.	54.75	48.97	1.5	....	86/42	
	7 yr. 2 mo.	60.5	52.0	....	4.2	.....	78/48
	8 yr.	64	54.13	....	7.7	.....	94/56
	9 yr.	71.5	56.29	....	7.2	.....	88/56
	10 yr.	74.25	58.74	....	13.8	.....	88/54
	11 yr.	83	61.22	....	17.0	.....	84/52
	12 yr.	97.75	63.93	....	14.0	.....	94/56
	12 yr. 11 mo.	110.25	65.8	....	10.5	92/64	88/60
	14 yr. 3 mo.	127	67	....	2.5	112/74	102/64
C. E.	4 yr. 5 mo.	37.75	41.33	0	0	64/48	
	5 yr. 6 mo.	43.75	43.97	4.2	....	90/62	
	6 yr. 5 mo.	47	46	0	0	86/60	
	7 yr. 7 mo.	52	48.3	....	1.4	.....	80/48
	8 yr. 5 mo.	56	50	....	2.6	.....	78/46
	9 yr. 7 mo.	60	51.65	....	4.6	.....	92/52
	10 yr. 5 mo.	62	53	....	8.8	.....	80/44
	11 yr. 5 mo.	68.25	55.23	....	9.5	.....	84/50
	12 yr. 4 mo.	77.25	57.6	....	9.5	98/50	84/48
	13 yr. 9 mo.	92.75	60.4	....	8.7	110/56	96/48
C. F.	5 yr. 5 mo.	51.25	44.48	18.0	....	80/56	
	3 yr. 5 mo.	61.75	47.28	22.1	....	92/60	
	7 yr. 5 mo.	68.75	50	21.1	....	.....	86/58
	8 yr. 5 mo.	82.25	52.16	27.5	....	.....	90/66
	9 yr. 3 mo.	93.5	54.6	29.1	....	.....	100/68
	10 yr. 3 mo.	108.75	58.26	26.6	....	.....	98/62
	11 yr. 3 mo.	109	60.78	11.0	....	.....	98/56
	12 yr. 4 mo.	128	61.6	24.2	....	.....	108/58
	13 yr. 5 mo.	128.25	62.4	17.7	....	.....	106/60
	14 yr. 5 mo.	129.5	62.4	15.4	....	.....	106/58
C. G.	5 yr.	35.25	39.76	0	0	82/52	
	5 yr. 11 mo.	38.75	42	0	0	92/62	
	7 yr.	41.75	43.93	0	0	96/50	
	7 yr. 11 mo.	45	45.82	....	5.1	90/48	
	8 yr. 10 mo.	48.5	47.36	....	4.3	.....	86/58
	9 yr. 10 mo.	54.75	50	....	8	.....	92/66
	11 yr. 2 mo.	59.5	52.67	....	11.1	.....	86/62
	11 yr. 11 mo.	71	55.23	....	6.5	.....	92/50
	12 yr. 11 mo.	82	58.1	....	7.2	88/54	84/56
	14 yr. 2 mo.	90.5	60	....	10.3	100/68	86/52

TABLE 5.—*Longitudinal Recordings on Individual Girls (Six Year Follow-Up)*

Subject	Age	Weight, Pounds	Height, Inches	Percentage		Blood Pressure Reading	
				Over Average Weight	Under Average Weight	Child Cuff	Adult Cuff
C. O.	4 yr. 1 mo.	35	38.97	2.9	....	78/56	
	4 yr. 11 mo.	38.5	41.22	2.9	....	86/54	
	5 yr. 11 mo.	44.25	43.7	6.1	....	84/62	
	6 yr. 11 mo.	50.75	46.25	6.2	....	88/58	70/52
	7 yr. 11 mo.	58.5	48.8	7.5	....	96/58	82/48
	8 yr. 11 mo.	67.5	51.6	7.4	....	104/60	88/58
C. P.	4 yr.	33.5	39.88	....	6.3	78/44	
	5 yr.	37.75	42.2	....	4.1	78/46	
	6 yr.	43.75	44.48	0	0	78/44	
	7 yr. 3 mo.	50.75	47	1.5	....	88/44	84/34
	8 yr. 5 mo.	59.5	49.7	5.2	....	94/52	88/40
	9 yr. 2 mo.	64.25	51.5	2.8	....	102/54	88/38

TABLE 6.—*Longitudinal Recordings for Individual Girls (Five Year Follow-Up)*

Subject	Age	Weight, Pounds	Height, Inches	Percentage		Blood Pressure Reading	
				Over Average Weight	Under Average Weight	Child Cuff	Adult Cuff
C. H.	5 yr. 7 mo.	45.5	44.76	2.3	....	88/56	
	6 yr. 8 mo.	57	47.83	10.3	....	86/66	
	7 yr. 11 mo.	72	50.1	25.6	....	94/52	88/58
	9 yr. 1 mo.	84	53.9	20.5	....	98/74	90/56
	9 yr. 7 mo.	87.75	54.5	21.8	....	102/64	90/58
C. I.	4 yr. 8 mo.	48	42.83	18	....	84/58	
	5 yr. 9 mo.	52.75	45.43	15	....	76/52	
	6 yr. 8 mo.	60	47.55	17.4	....	86/52	78/50
	8 yr. 3 mo.	67.75	51.9	6.5	....	96/62	82/56
	8 yr. 10 mo.	72.25	53.3	6.4	....	86/58	82/54
C. J.	5 yr. 4 mo.	44.25	45.35	....	3.1	82/48	
	6 yr. 4 mo.	49.75	47.87	....	3.8	88/62	
	7 yr. 7 mo.	55.75	50.6	....	4.4	96/74	82/?
	8 yr. 9 mo.	66	53.2	....	2.3	98/60	88/?
	9 yr. 5 mo.	70.5	54.4	1.5	....	96/64	78/52
C. K.	4 yr. 5 mo.	42.75	43.26	1.1	....	86/50	
	5 yr. 5 mo.	50	46.18	5.3	....	84/56	
	6 yr. 8 mo.	61.5	49.7	11	....	94/68	80/58
	7 yr. 5 mo.	68.25	52	7.3	....	84/60	74/48
	8 yr. 5 mo.	76.25	54.9	5	....	92/60	86/64
C. L.	4 yr. 9 mo.	39.25	40.7	6.9	....	96/58	
	5 yr. 10 mo.	45.5	43.46	9.7	....	98/68	
	7 yr.	52.25	46.5	7.7	....	102/66	96/48
	8 yr. 2 mo.	61.25	49.5	11.1	....	106/68	100/66
	8 yr. 10 mo.	68	50.8	10.9	....	112/72	92/64
A. C.	4 yr. 1 mo.	37.25	40.59	3.4	....	82/52	
	4 yr. 5 mo.	39.25	41.81	1.6	....	74/52	
	5 yr. 5 mo.	45.25	44.52	3.8	....	86/52	84/46
	6 yr. 7 mo.	52.5	46.7	6.4	....	96/58	84/52
	7 yr. 9 mo.	62.5	49.7	11.8	....	102/62	92/58
C. M.	4 yr. 9 mo.	47.25	44.33	9.8	....	90/52	
	5 yr. 10 mo.	54.25	47.79	5.1	....	86/54	
	6 yr. 11 mo.	62	50.5	7.8	....	90/64	80/58
	8 yr. 2 mo.	71.25	53.6	4.4	....	90/68	84/66
	8 yr. 10 mo.	75.75	55.1	2	....	98/62	82/54
C. N.	5 yr.	33	41.41	....	12.1	92/54	
	5 yr. 8 mo.	37.25	42.79	....	8.2	80/52	
	6 yr. 10 mo.	44.25	46.2	....	7.1	80/60	72/48
	8 yr. 1 mo.	49.25	48.8	....	9.4	88/60	78/56
	8 yr. 8 mo.	53	50	....	7.8	84/50	80/50

palpatory and oscillatory methods for systolic and the oscillatory for diastolic pressures. His results were stated in centimeters of water and have been converted into millimeters of mercury for tables 1, 2 and 3.

TABLE 7.—*Ranges with Child Cuff at Increasing Age Levels*

Age, Years	No. of Cases	Weight, Pounds	Height, Inches	Percentage Over or Under Average Weight	Blood Pressure, Mm. Hg	
					Systolic	Diastolic
4	30	30.00 to 42.00	37.4 to 45.6	12.8 under to 8.0 over	58 to 92	40 to 68
4½	44	30.25 to 57.00	39.0 to 45.9	14.0 under to 22.6 over	56 to 108	32 to 72
5	63	33.00 to 67.00	39.7 to 48.0	17.9 under to 45.3 over	68 to 104	42 to 74
5½	88	35.00 to 62.70	40.9 to 48.8	10.3 under to 37.6 over	68 to 106	34 to 74
6	78	33.20 to 60.70	41.4 to 49.8	18.0 under to 29.6 over	74 to 108	42 to 78
6½	87	40.50 to 79.50	43.1 to 51.0	14.5 under to 48.3 over	76 to 108	46 to 76
7	49	37.00 to 75.20	43.7 to 51.9	17.3 under to 31.9 over	80 to 108	44 to 72
7½	46	43.50 to 90.00	46.1 to 53.9	13.7 under to 53.5 over	84 to 118	48 to 82
8	36	45.00 to 79.70	45.8 to 54.4	17.0 under to 41.4 over	84 to 116	48 to 84
8½	22	48.50 to 92.25	47.5 to 56.7	19.0 under to 18.4 over	80 to 116	50 to 78
9	28	51.20 to 91.50	48.5 to 56.1	20.0 under to 24.2 over	80 to 118	52 to 80
9½	11	54.00 to 89.70	49.6 to 56.7	16.4 under to 28.6 over	92 to 118	58 to 74
10	9	60.50 to 90.00	50.4 to 58.8	18.4 under to 34.7 over	80 to 114	52 to 70
10½	5	58.00 to 106.70	52.4 to 59.2	14.9 under to 20.2 over	96 to 110	60 to 74
11	6	63.50 to 94.50	53.3 to 60.6	17.7 under to 29.2 over	96 to 116	56 to 74
11½	9	61.50 to 166.00	51.7 to 63.5	10.8 under to 48.2 over	96 to 138	54 to 86
12	1	.....	.....	.....	.....	.....
12½	4	77.25 to 116.50	57.6 to 64.5	9.5 under to 16.0 over	98 to 120	50 to 74
13	6	82.00 to 128.20	58.1 to 66.0	10.5 under to 16.5 over	88 to 114	54 to 78
13½	10	103.70 to 159.50	61.1 to 65.2	Neither to 37.4 over	102 to 124	64 to 88
14	9	85.00 to 144.50	60.0 to 68.0	17.1 under to 8.7 over	98 to 124	56 to 86
14½	8	102.00 to 154.00	62.4 to 67.0	8.2 under to 22.8 over	94 to 136	64 to 74
15	2	105.50 to 109.00	62.2 to 64.1	10.9 under to 4.0 under	110 to 116	68 to 72
15½	0	.....	.....	.....	.....	.....
16	0	.....	.....	.....	.....	.....

TABLE 8.—*Ranges with Adult Cuff at Increasing Age Levels*

Age, Years	No. of Cases	Weight, Pounds	Height, Inches	Percentage Over or Under Average Weight	Blood Pressure, Mm. Hg	
					Systolic	Diastolic
4¼	4	35.00 to 46.50	41.6 to 45.6	9.3 under to 13.1 over	72 to 80	52 to 58
5	11	37.70 to 67.00	42.2 to 47.6	5.5 under to 45.3 over	68 to 88	32 to 64
5½	20	36.70 to 66.20	41.6 to 50.0	13.6 under to 21.7 over	68 to 94	42 to 66
6	34	38.50 to 60.50	42.6 to 50.1	12.4 under to 29.6 over	66 to 100	46 to 70
6½	55	40.70 to 79.50	44.3 to 52.9	14.5 under to 48.3 over	66 to 102	38 to 78
7	51	42.20 to 82.50	45.3 to 53.1	14.1 under to 32.0 over	68 to 102	34 to 76
7½	79	45.70 to 93.00	45.9 to 55.2	18.0 under to 53.5 over	70 to 108	44 to 78
8	76	46.00 to 95.20	46.2 to 56.1	17.0 under to 41.7 over	70 to 110	42 to 74
8½	85	50.50 to 105.20	47.5 to 57.1	19.0 under to 43.4 over	72 to 114	40 to 76
9	79	45.50 to 114.00	47.3 to 58.5	20.0 under to 36.8 over	70 to 114	38 to 72
9½	74	51.70 to 122.20	49.3 to 59.6	16.4 under to 50.0 over	74 to 110	44 to 76
10	57	57.00 to 123.00	50.0 to 62.2	18.4 under to 38.0 over	72 to 120	48 to 72
10½	64	55.20 to 140.00	51.0 to 61.9	20.9 under to 40.0 over	80 to 114	44 to 84
11	43	59.50 to 143.70	52.6 to 65.4	17.7 under to 38.1 over	84 to 110	44 to 76
11½	57	61.50 to 166.00	51.7 to 64.3	16.1 under to 48.2 over	82 to 114	42 to 80
12	40	59.50 to 163.70	54.6 to 67.5	18.9 under to 31.4 over	84 to 120	48 to 82
12½	43	69.70 to 149.70	56.0 to 66.3	17.5 under to 33.7 over	84 to 116	46 to 78
13	32	71.70 to 172.00	56.5 to 68.3	14.8 under to 31.0 over	82 to 116	52 to 78
13½	31	88.20 to 159.50	57.3 to 66.5	12.9 under to 37.4 over	92 to 122	52 to 76
14	27	85.00 to 185.70	59.4 to 68.4	17.1 under to 38.7 over	86 to 126	48 to 86
14½	28	92.50 to 154.00	60.6 to 67.0	18.4 under to 22.8 over	86 to 120	56 to 76
15	15	94.50 to 140.00	60.2 to 66.3	13.8 under to 19.4 over	94 to 114	50 to 74
15½	13	98.00 to 203.70	61.0 to 68.9	14.6 under to 48.9 over	92 to 122	56 to 72
16	5	110.20 to 125.70	61.2 to 64.5	4.6 under to 4.0 over	94 to 106	54 to 68

Faber and James [16] studied blood pressures of 651 boys and 450 girls. They found greater standard deviations in girls than in boys, especially

16. Faber, H. K., and James, C. A.: The Range and Distribution of Blood Pressures in Normal Children, Am. J. Dis. Child. **22:7** (July) 1921.

during adolescence. Burlage [17] worked on girls from 9 to 26 years old and found the systolic pressure to increase with age up to puberty and then to vary only slightly up to 26 years. Lincoln [18] found pulse pressure to increase only slightly with age. Meyer [19] studied blood pressures of 320 school children from 6 to 14 years old, pronounced by the school physician and the teacher to be normal. Blood pressures

TABLE 9.—*Ranges with Child Cuff at Increasing Weights*

Weight, Pounds	No. of Cases	Age, Years	Height, Inches	Percentage Over or Under Average Weight	Blood Pressure, Mm. Hg	
					Systolic	Diastolic
30.0 to 39.9	97	3 7/12 to 6 9/12	37.4 to 45.9	18.0 under to 8.0 over	56 to 98	32 to 68
40.0 to 49.9	217	3 11/12 to 8 6/12	40.8 to 49.6	17.3 under to 26.1 over	68 to 108	34 to 76
50.0 to 59.9	155	4 3/12 to 10 6/12	43.3 to 55.1	20.0 under to 31.0 over	76 to 116	38 to 80
60.0 to 69.9	82	4 11/12 to 11 8/12	44.8 to 57.7	18.4 under to 45.3 over	80 to 118	48 to 84
70.0 to 79.9	32	6 5/12 to 12 4/12	47.3 to 58.5	10.8 under to 48.3 over	86 to 118	50 to 78
80.0 to 89.9	19	7 7/12 to 14	52.4 to 60.6	17.1 under to 28.6 over	88 to 118	54 to 78
90.0 to 99.9	9	7 4/12 to 14 2/12	50.7 to 60.6	10.3 under to 53.5 over	88 to 116	52 to 82
100.0 to 109.9	8	10 4/12 to 15 1/12	56.6 to 64.1	10.9 under to 34.6 over	94 to 116	66 to 78
110.0 to 119.9	12	11 6/12 to 14 5/12	59.0 to 66.0	10.5 under to 22.2 over	92 to 124	58 to 82
120.0 to 129.9	11	13 2/12 to 14 4/12	63.0 to 67.0	2.5 under to 16.5 over	98 to 124	60 to 78
130.0 to 139.9	3	13 8/12 to 14 8/12	62.4 to 64.2	14.2 over to 19.7 over	104 to 122	64 to 78
140.0 to 149.9	3	11 10/12 to 14 5/12	63.0 to 68.0	7.4 over to 30.2 over	118 to 136	64 to 86
150.0 to 159.9	2	13 6/12 to 14 6/12	64.0 to 66.7	19.6 over to 37.4 over	110 to 134	66 to 80
160.0 to 169.9	1	.....	.....	.....	.....	.....

TABLE 10.—*Ranges with Adult Cuff at Increasing Weights*

Weight, Pounds	No. of Cases	Age, Years	Height, Inches	Percentage Over or Under Average Weight	Blood Pressure, Mm. Hg	
					Systolic	Diastolic
30.0 to 39.9	10	4 4/12 to 5 11/12	41.6 to 44.3	10.3 under to 4.1 over	68 to 94	44 to 58
40.0 to 49.9	82	4 5/12 to 8 10/12	42.5 to 49.6	17.0 under to 13.1 over	66 to 98	32 to 76
50.0 to 59.9	169	5 4/12 to 11 9/12	44.2 to 55.1	20.9 under to 29.6 over	68 to 108	34 to 78
60.4 to 69.9	194	4 11/12 to 12 8/12	45.5 to 57.7	18.4 under to 45.3 over	72 to 110	38 to 78
70.0 to 79.9	138	6 6/12 to 12 9/12	47.3 to 59.0	13.8 under to 48.3 over	76 to 112	52 to 78
80.0 to 89.9	120	7 to 14 1/12	50.4 to 61.6	17.5 under to 41.7 over	82 to 118	46 to 76
90.0 to 99.9	89	7 3/12 to 15 4/12	50.7 to 64.0	18.4 under to 53.5 over	76 to 120	44 to 78
100.0 to 109.9	83	8 4/12 to 15 7/12	55.1 to 68.0	13.8 under to 43.4 over	86 to 116	52 to 82
110.0 to 119.9	68	9 1/12 to 16 1/12	58.0 to 67.0	11.0 under to 37.9 over	88 to 116	44 to 86
120.0 to 129.9	34	9 4/12 to 15 9/12	57.4 to 67.0	5.5 under to 50.0 over	90 to 120	46 to 76
130.0 to 139.9	12	11 2/12 to 15 2/12	60.0 to 66.6	2.0 over to 38.1 over	86 to 122	52 to 72
140.0 to 149.9	13	10 8/12 to 15 5/12	61.9 to 68.0	7.4 over to 35.2 over	90 to 120	52 to 84
150.0 to 159.9	5	13 2/12 to 15 6/12	64.0 to 66.7	19.6 over to 37.4 over	94 to 114	62 to 76
160.0 to 169.9	2	11 8/12 to 12	63.5 to 67.5	28.3 over to 48.2 over	114	48 to 76

were found to increase with increasing age, weight and height and to approach the adult levels at 14 years. Sundal [20] used 1,049 boys and 883

17. Burlage, S. R.: The Blood Pressure and Heart Rate in Girls During Adolescence, Am. J. Physiol. **64**:252 (April) 1923.

18. Lincoln, E. M.: Hearts of Normal Children: Clinical Studies, Including Notes on Effort Syndrome, Am. J. Dis. Child. **35**:398 (March) 1928.

19. Meyer, E.: Blood Pressure Research in Healthy and Sick Children, Ztschr. f. Kinderh. **47**:560, 1929.

20. Sundal, A.: Normal Blood Pressure in Children 3-20 Years: Research on 1932 Children and Young Adults in Oslo, Norway, Ztschr. f. Kinderh. **47**:742, 1929.

TABLE 11.—*Ranges with Child Cuff at Increasing Heights*

Height, Inches	No. of Cases	Age, Years	Weight, Pounds	Percentage Over or Under Average Weight	Blood Pressure, Mm. Hg	
					Systolic	Diastolic
36 to 37.99	3	3 9/12 to 3 10/12	30.75 to 35.25	2.0 under to 6.0 over	74 to 84	48 to 62
38 to 39.99	22	3 9/12 to 5	30.00 to 37.50	12.8 under to 5.3 over	58 to 92	40 to 68
40 to 41.99	44	3 7/12 to 5 9/13	33.00 to 43.25	12.4 under to 16.3 over	56 to 96	32 to 68
42 to 43.99	76	3 11/12 to 7	33.25 to 52.00	18.0 under to 26.1 over	74 to 100	34 to 72
44 to 45.99	115	3 11/12 to 7 11/12	36.75 to 59.25	17.9 under to 45.3 over	68 to 108	38 to 72
46 to 47.99	125	5 to 8 4/12	40.25 to 73.25	17.3 under to 41.4 over	76 to 108	44 to 78
48 to 49.99	87	5 to 9 4/12	45.75 to 74.50	14.5 under to 48.3 over	80 to 110	42 to 74
50 to 51.99	56	6 5/12 to 11 8/12	48.75 to 90.00	17.0 under to 53.5 over	82 to 118	46 to 76
52 to 53.99	41	7 5/12 to 11	54.75 to 90.00	16.4 under to 34.7 over	84 to 118	56 to 84
54 to 55.99	22	7 9/12 to 10 11/12	58.50 to 94.50	20.0 under to 29.2 over	80 to 116	52 to 80
56 to 57.99	10	8 7/12 to 12 4/12	57.00 to 108.50	18.4 under to 34.6 over	88 to 114	50 to 78
58 to 59.99	6	10 to 12 11/12	58.80 to 110.00	10.8 under to 22.2 over	88 to 114	54 to 74
60 to 61.99	10	10 11/12 to 14 2/12	85.00 to 119.75	17.1 under to 16.0 over	100 to 122	56 to 82
62 to 63.99	17	11 8/12 to 15 1/12	102.00 to 166.00	8.2 under to 48.2 over	94 to 138	60 to 86
64 to 65.99	10	12 3/12 to 14 10/12	105.50 to 159.50	10.9 under to 37.4 over	92 to 120	64 to 80
66 to 67.99	5	13 1/12 to 14 6/12	119.50 to 154.00	3.7 under to 19.6 over	104 to 134	66 to 86

TABLE 12.—*Ranges with Adult Cuff at Increasing Heights*

Height, Inches	No. of Cases	Age, Years	Weight, Pounds	Percentage Over or Under Average Weight	Blood Pressure, Mm. Hg	
					Systolic	Diastolic
40 to 41.99	2	4 9/12 to 5 7/12	35.00 to 38.50	9.3 under to average	68 to 80	44 to 52
42 to 43.99	14	4 4/12 to 6 2/12	36.75 to 45.25	10.3 under to 13.1 over	68 to 92	32 to 58
44 to 45.99	28	4 5/12 to 7 4/12	39.25 to 55.25	12.4 under to 45.3 over	66 to 98	42 to 62
46 to 47.99	74	5 3/12 to 8 10/12	41.00 to 73.25	15.4 under to 41.4 over	70 to 100	34 to 70
48 to 49.99	104	5 7/13 to 9 5/12	45.25 to 71.75	14.5 under to 48.3 over	66 to 100	40 to 78
50 to 51.99	147	5 4/12 to 11 8/12	48.75 to 90.00	17.0 under to 53.5 over	72 to 106	38 to 78
52 to 53.99	144	7 to 11 3/12	52.75 to 94.00	20.9 under to 43.0 over	70 to 110	42 to 74
54 to 55.99	110	7 4/12 to 12 2/12	58.50 to 105.50	20.0 under to 43.4 over	72 to 114	42 to 76
56 to 57.99	83	8 2/12 to 13 4/12	57.00 to 122.25	18.4 under to 50.0 over	76 to 110	48 to 74
58 to 59.99	73	9 1/12 to 14 1/12	58.80 to 118.75	13.8 under to 37.9 over	82 to 118	44 to 78
60 to 61.99	88	10 to 16	82.50 to 136.75	17.5 under to 38.1 over	84 to 120	46 to 78
62 to 63.99	87	10 1/13 to 16	93.25 to 166.00	14.8 under to 48.2 over	82 to 122	52 to 86
64 to 65.99	45	11 to 15 9/12	104.50 to 159.50	18.4 under to 37.4 over	86 to 114	52 to 80
66 to 67.99	19	12 to 15 9/12	108.25 to 163.75	13.5 under to 28.3 over	89 to 114	50 to 78

TABLE 13.—*Averages with Child Cuff at Increasing Age Levels*

Age, Years	No. of Cases	Weight, Pounds	Height, Inches	Percentage Over or Under Average Weight	Blood Pressure, Mm. Hg	
					Systolic	Diastolic
4	30	35.7	40.3	1.2 under	80.0	54.6
4½	44	39.8	41.9	2.1 over	83.0	55.4
5	63	42.5	43.3	2.5 over	86.0	55.0
5½	88	47.0	45.0	4.2 over	88.1	56.3
6	78	47.5	45.8	1.1 over	90.2	59.0
6½	87	53.1	47.4	5.0 over	92.0	61.0
7	49	52.6	47.9	1.7 over	92.6	58.7
7½	46	59.1	49.8	4.0 over	96.4	63.5
8	36	58.9	50.0	1.8 over	96.5	64.0
8½	22	69.2	51.9	1.7 over	98.0	63.5
9	28	70.3	53.0	4.8 over	100.3	64.7
9½	11	72.7	52.8	8.9 over	100.7	66.0
10	9	72.6	54.6	0.4 over	97.0	61.0
10½	5	74.6	54.6	1.0 over	104.0	65.0
11	6	79.0	56.3	Neither	106.6	65.6
11½	9	98.2	58.2	9.9 over	110.6	70.9
12	1	.....	....	.....	.....	....
12½	4	105.3	61.4	2.5 over	110.5	64.0
13	6	109.9	63.3	1.9 under	102.0	65.6
13½	10	124.9	63.2	11.2 over	112.0	73.8
14	9	112.4	62.7	0.1 over	111.0	69.7
14½	8	130.2	64.9	6.9 over	112.0	67.2
15	2	107.2	63.1	7.4 under	113.0	69.0
15½	0	.....	....	.....	.....	....
16	0	.....	....	.....	.....	....

TABLE 14.—*Averages with Adult Cuff at Increasing Age Levels*

Age, Years	No. of Cases	Weight, Pounds	Height, Inches	Percentage Over or Under Average Weight	Blood Pressure, Mm. Hg	
					Systolic	Diastolic
4½	4	41.1	43.0	0.8 over	75.5	55.0
5	11	45.0	44.0	5.9 over	76.0	53.0
5½	20	47.4	45.7	0.9 over	78.2	53.0
6	34	49.2	46.6	0.9 over	84.2	56.2
6½	55	53.9	48.2	2.8 over	83.9	57.0
7	51	55.8	48.8	3.0 over	84.1	55.6
7½	79	62.1	50.3	6.5 over	88.0	58.5
8	76	62.8	50.9	4.1 over	88.6	57.8
8½	85	68.3	52.1	6.1 over	90.0	58.2
9	79	71.6	53.2	5.2 over	90.8	58.7
9½	74	74.8	53.8	6.2 over	92.0	58.5
10	57	79.6	55.3	5.5 over	94.0	58.9
10½	64	84.0	56.6	3.6 over	94.5	60.0
11	43	89.4	57.4	5.3 over	95.8	59.7
11½	57	94.4	58.9	3.6 over	97.5	62.0
12	40	99.3	60.1	2.5 over	100.1	61.3
12½	43	104.6	61.6	3.0 over	101.4	62.0
13	32	109.1	62.2	1.6 over	100.1	62.4
13½	31	114.6	62.8	3.9 over	102.7	64.0
14	27	112.8	63.0	0.5 under	99.8	63.4
14½	28	117.0	63.9	0.3 under	98.8	63.8
15	15	113.5	63.8	3.7 under	104.0	62.6
15½	13	126.6	64.8	2.3 over	103.4	63.5
16	5	117.2	62.9	0.1 over	100.4	61.0

TABLE 15.—*Averages with Child Cuff at Increasing Weights*

Weight, Pounds	No. of Cases	Age, Years	Height, Inches	Percentage Over or Under Average Weight	Blood Pressure, Mm. Hg	
					Systolic	Diastolic
30 to 39.9	97	4 8/12	41.2	2.8 under	82.0	54.7
40 to 49.9	217	6 5/12	45.2	0.6 under	88.5	58.0
50 to 59.9	155	6 9/12	48.3	3.7 over	92.8	60.6
60 to 69.9	82	7 9/12	50.7	8.8 over	96.9	63.6
70 to 79.9	32	8 11/12	53.0	11.8 over	102.3	64.6
80 to 89.9	19	10	55.6	11.9 over	107.0	66.7
90 to 99.9	9	10 5/12	56.3	16.7 over	108.1	66.0
100 to 109.9	8	13	61.0	4.9 over	107.5	69.7
110 to 119.9	12	13	63.3	3.6 over	111.6	69.0
120 to 129.9	11	13 8/12	64.3	6.7 over	108.7	70.4
130 to 139.9	3	14 3/12	63.6	16.1 over	111.3	72.0
140 to 149.9	3	13 4/12	64.9	20.1 over	128.0	78.6
150 to 159.9	2	14	65.3	28.5 over	122.0	73.0
160 to 169.9	1	.....	....	.....	.....	....

TABLE 16.—*Averages with Adult Cuff at Increasing Weights*

Weight, Pounds	No. of Cases	Age, Years	Height, Inches	Percentage Over or Under Average Weight	Blood Pressure, Mm. Hg	
					Systolic	Diastolic
30 to 39.9	10	5 4/12	42.6	4.7 under	77.2	51.5
40 to 49.9	82	6 5/12	46.4	5.1 under	80.9	55.2
50 to 59.9	169	7 8/12	49.5	1.4 under	85.8	56.5
60 to 69.9	194	8 6/12	52.0	2.4 over	89.2	58.3
70 to 79.9	138	9 6/12	54.3	4.3 over	91.9	58.8
80 to 89.9	120	10 3/12	56.4	8.4 over	95.6	60.0
90 to 99.9	89	11 4/12	58.9	6.5 over	97.1	60.0
100 to 109.9	83	12 3/12	61.0	5.1 over	100.2	63.2
110 to 119.9	68	13 4/12	62.8	4.7 over	101.3	63.8
120 to 129.9	34	13 2/12	63.4	11.9 over	102.9	63.0
130 to 139.9	12	13 5/12	63.1	20.4 over	100.8	62.3
140 to 149.9	12	13	64.6	22.3 over	108.4	69.2
150 to 159.9	5	14 2/12	65.3	27.7 over	108.0	69.0
160 to 169.9	2	11 10/12	65.5	38.2 over	114.0	62.0

girls, 3 to 20 years old. Blood pressure was found to rise comparatively faster in girls 9 to 12 years old and in boys 10 to 13 years old. There was no further increase in girls after 15 years and in boys after 17 years. In children of the same age, the blood pressure was higher in taller and heavier children. Chabrun and Petrovitch [21] used both the auscultatory method with the Vaquez-Laubry instrument and a 5 cm. cuff for children 4 to 12 years old and a 12 cm. cuff for children 12 to 15 years

TABLE 17.—*Averages with Child Cuff at Increasing Heights*

Height, Inches	No. of Cases	Age, Years	Weight, Pounds	Percentage Over or Under Average Weight	Blood Pressure, Mm. Hg	
					Systolic	Diastolic
36 to 37.99	3	3 9/12	33.6	4.0 over	80.0	55.0
38 to 39.99	22	4 2/12	33.8	2.4 under	78.4	53.0
40 to 41.99	44	4 7/12	37.7	0.8 over	83.0	55.4
42 to 43.99	76	5 2/12	41.4	2.0 over	85.1	56.6
44 to 45.99	115	5 7/12	45.6	1.9 over	88.4	56.5
46 to 47.99	125	6 4/12	50.9	2.6 over	91.3	60.0
48 to 49.99	87	7	56.4	5.5 over	94.4	61.1
50 to 51.99	56	7 1/12	61.5	3.6 over	96.7	63.2
52 to 53.99	41	8 9/12	69.5	3.9 over	101.2	65.6
54 to 55.99	22	9 3/12	74.1	2.8 over	101.6	67.2
56 to 57.99	10	10 3/12	81.0	4.7 over	102.2	64.0
58 to 59.99	6	11 3/12	86.9	2.4 over	104.6	61.3
60 to 61.99	10	12 11/12	100.6	0.6 under	111.2	69.6
62 to 63.99	17	13 5/12	124.7	11.0 over	113.9	71.7
64 to 65.99	10	13 8/12	124.2	4.5 over	109.4	69.8
66 to 67.99	5	14	134.5	3.6 over	114.8	74.0

TABLE 18.—*Averages with Adult Cuff at Increasing Heights*

Height, Inches	No. of Cases	Age, Years	Weight, Pounds	Percentage Over or Under Average Weight	Blood Pressure, Mm. Hg	
					Systolic	Diastolic
36 to 37.99	0	.....	....	.....	....	....
38 to 39.99	0	.....	....	.....	....	....
40 to 41.99	2	5 2/12	36.7	4.6 under	74.0	48.0
42 to 43.99	14	5 2/12	40.0	0.6 under	75.5	52.6
44 to 45.99	28	5 10/12	46.1	2.2 over	79.0	52.9
46 to 47.99	74	6 8/12	50.7	1.5 over	83.1	55.4
48 to 49.99	104	7 4/12	55.4	2.4 over	85.2	57.0
50 to 51.99	147	8 2/12	62.8	4.8 over	88.6	58.4
52 to 53.99	144	8 11/12	70.4	5.3 over	91.2	58.4
54 to 55.99	110	9 8/12	76.7	4.7 over	93.1	59.3
56 to 57.99	83	10 5/12	85.1	5.8 over	95.5	59.9
58 to 59.99	73	11 1/12	93.5	5.6 over	96.0	60.0
60 to 61.99	88	12 5/12	103.6	2.8 over	99.5	62.0
62 to 63.99	87	13 3/12	113.5	2.2 over	102.3	64.0
64 to 65.99	45	14	120.2	0.9 over	103.2	64.7
66 to 67.99	19	14	130.1	1.8 over	103.1	63.0

old and also the oscillometer of Pachon and an 8 cm. cuff. They found little variation with weight in children of the same age, but a gradual increase with age, a little faster at puberty. Richey [22] expressed the opinion that blood pressures react noticeably to forces which do not

21. Chabrun, J., and Petrovitch, Y.: Study of the Blood Pressure in the Normal Child Between 4 and 15 Years, Arch. de méd. d. enf. **33**:601 (Oct.) 1930.

22. Richey, H. G.: The Blood Pressure in Boys and Girls Before and After Puberty: Its Relation to Growth and to Maturity, Am. J. Dis. Child. **42**:1281 (Dec.) 1931.

TABLE 19.—*Ranges with Child and Adult Cuffs at Increasing Weights*

Weight, Pounds	No. of Cases	Age, Years	Height, Inches	Percentage Over or Under Average Weight	Blood Pressure, Mm. Hg	
					Child Cuff	Adult Cuff
30 to 39.9	10	4 4/12 to 5 11/12	41.6 to 44.3	10.3 under to 4.1 over	80 - 98/52 - 68	68 - 94/44 - 58
40 to 49.9	62	4 8/12 to 8 2/12	42.5 to 50.5	17.0 under to 13.1 over	74 - 108/46 - 72	66 - 98/32 - 68
50 to 59.9	78	5 4/12 to 10 6/12	44.2 to 55.1	20.0 under to 29.6 over	80 - 116/44 - 78	70 - 108/34 - 72
60 to 69.9	61	4 11/12 to 11 8/12	45.5 to 57.7	18.4 under to 45.3 over	80 - 118/50 - 78	72 - 106/38 - 78
70 to 79.9	30	6 6/12 to 12 4/12	47.3 to 58.5	10.8 under to 48.3 over	86 - 118/50 - 78	78 - 106/48 - 68
80 to 89.9	19	8 6/12 to 14	52.4 to 60.6	17.1 under to 28.6 over	92 - 118/54 - 78	84 - 108/50 - 76
90 to 99.9	9	7 4/13 to 14 2/12	50.7 to 60.6	10.3 under to 53.5 over	88 - 116/52 - 82	76 - 102/44 68
100 to 109.9	8	10 4/12 to 15 1/12	56.6 to 64.1	10.9 under to 34.6 over	94 - 116/66 - 78	86 - 108/60 - 74
110 to 119.9	12	11 6/12 to 14 5/12	59.0 to 66.0	10.5 under to 22.2 over	92 - 124/58 - 82	88 - 114/44 - 86
120 to 129.9	11	13 2/12 to 14 4/12	63.0 to 67.0	2.5 under to 16.5 over	98 - 124/60 - 78	90 - 112/58 - 76
130 to 139.9	3	13 8/12 to 14 8/12	62.4 to 64.2	14.2 over to 19.7 over	104 - 122/64 - 78	86 - 106/56 - 68
140 to 149.9	3	11 10/12 to 14 5/12	63.0 to 68.0	7.4 over to 30.2 over	118 - 136/64 - 86	110 - 120/66 - 82
150 to 159.9	2	13 6/12 to 14 6/12	64.0 to 66.7	19.6 over to 37.4 over	110 - 134/66 - 80	94 - 114/72 - 76
160 to 169.9	1	.....	.....	.....	.....	.....

TABLE 20.—*Averages with Child and Adult Cuffs at Increasing Weights*

Weight, Pounds	No. of Cases	Age, Years	Height, Inches	Percentage Over or Under Average Weight	Blood Pressure, Mm. Hg	
					Child Cuff	Adult Cuff
30 to 39.9	10	5 4/12	42.6	4.7 under	87.2/59.8	77.2/51.5
40 to 49.9	62	6 3/12	46.2	4.5 under	90.7/59.5	79.1/54.6
50 to 59.9	78	7 3/12	49.0	0.2 under	93.7/62.8	85.5/57.4
60 to 69.9	61	8 3/12	51.5	4.6 over	98.3/64.7	87.5/59.7
70 to 79.9	30	8 9/12	53.1	10.5 over	102.2/64.5	89.9/59.3
80 to 89.9	19	9 5/12	55.6	11.9 over	107.1/66.7	95.9/61.2
90 to 99.9	9	10 5/12	56.3	16.7 over	103.1/66.0	92.2/57 1
100 to 109.9	8	13	61.0	4.9 over	107.5/69.7	98.0/64.7
110 to 119.9	12	13 1/12	63.3	3.6 over	111.6/69.1	100.5/63.0
120 to 129.9	11	13 8/12	64.3	6.7 over	108.7/70.4	101.6/68.7
130 to 139.9	3	14 3/12	63.6	16.1 over	111.3/72.0	96.0/63.3
140 to 149.9	3	13 4/12	64.9	20.1 over	128.0/78.6	115.3/75.3
150 to 159.9	2	14	65.3	48.2 over	122.0/73.0	104.0/74.0
160 to 169.9	1	.....	....	.....	.....	.....

TABLE 21.—*Averages of Blood Pressure of Girls More than 10 Per Cent Under and More than 15 Per Cent Over Average Weight*

Height, Inches	More Than 10% Underweight		More Than 15% Overweight	
	Child Cuff	Adult Cuff	Child Cuff	Adult Cuff
40 to 41.99	91 / 59	.....	92 /?	
42 to 43.99	84 / 55	.....	87.5/ 59.5	
44 to 45.99	86.5/ 55	.....	96.5/ 59.7	
46 to 47.99	89 / 58	88 / 56	94 / 61	85.4 / 53.4
48 to 49.99	90 / 57	82.2/ 53.8	96 / 61.4	88.7 / 58
50 to 51.99	94 / 61.6	86 / 56.3	103 / 68	91 / 61.3
52 to 53.99	99 / 65	83 / 59	108.8/ 66.6	95.7/ 59.6
54 to 55.99	106 / 72	93.8/ 61.8	102.5/ 67	95.7/ 61.5
56 to 57.99	98 / 64	94.5/ 59	100 / 66	97.3/ 61.1
58 to 59.99	98 / 54	94.5/ 60.7	110 / 70	98 / 60.7
60 to 61.99	107 / 73	98 / 62	112 / 73	102.6/ 63
62 to 63.99	.....	97.4/ 61	126 / 75	107.5/ 63
64 to 65.99	104 / 66	101.5/ 61.7	110 / 80	103.7/ 66.5

TABLE 22.—*Table of Least and Greatest Differences Between Readings with Child and Adult Cuff*

Height, Inches	Subject	Age, Years	Weight, Pounds	Percentage Over or Under Average Weight	Difference
		Least Difference			
40 to 41.99	A. A.	4 9/12	35.00	9.3 under	4
42 to 43.99	A. B.	5 2/12	39.00	5.5 under	2
44 to 45.99	A. C.	5 5/12	45.25	3.8 over	2
	A. D.	5 10/12	44.00	2.2 under	2
46 to 47.99	A. E.	6 5/12	53.75	3.7 over	0
	A. F.	6 6/12	50.00	1.7 under	0
	A. G.	6	59.25	22.7 over	0
48 to 49.99	A. H.	6 4/12	52.00	6.4 under	2
	A. I.	6 11/12	52.00	4.7 under	2
50 to 51.99	A. J.	9 3/12	54.00	7.8 under	0
	A. K.	9 3/12	69.50	10.1 over	0
	A. F.	7 6/12	57.75	2.2 over	0
52 to 53.99	A. L.	9 11/12	63.25	7.0 under	0
	A. E.	7 11/12	68.00	6.2 over	0
	A. M.	8 10/12	66.50	1.7 under	0
	A. N.	7 7/12	64.50	Neither	0
54 to 55.99	A. O.	8 9/12	80.25	24.2 over	2
56 to 57.99	A. O.	9 4/12	89.50	12.8 over	6
	A. P.	8 7/12	92.25	18.4 over	6
58 to 59.99	A. Q.	11 9/12	78.50	10.8 under	0
60 to 61.99	A. R.	13 8/12	108.75	Neither	8
62 to 63.99	A. S.	13 7/12	114.00	Neither	2
64 to 65.99	A. T.	14 5/12	119.00	2.5 under	4
	A. U.	12 11/12	110.25	10.5 under	4
66 to 67.99	A. V.	13 10/12	144.50	7.4 over	8
		Greatest Difference			
40 to 41.99	B. A.	5 7/12	38.50	Neither	14
42 to 43.99	B. B.	5 6/12	37.00	10.0 under	28
44 to 45.99	B. C.	4 11/12	67.00	45.3 over	22
46 to 47.99	B. D.	7 1/12	64.00	31.9 over	24
	B. E.	6 5/12	47.50	3.7 under	24
48 to 49.99	B. F.	7 1/12	49.75	Neither	32
50 to 51.99	B. G.	8 7/12	73.25	17.6 over	24
52 to 53.99	B. G.	9 4/12	82.50	24.2 over	22
54 to 55.99	B. H.	8 6/12	61.00	13.9 under	22
56 to 57.99	B. I.	8 9/12	70.75	6.2 under	18
58 to 59.99	B. J.	11 3/12	85.50	3.7 under	22
60 to 61.99	B. K.	13 8/12	119.75	15.1 over	26
62 to 63.99	B. L.	11 8/12	166.00	48.2 over	24
64 to 65.99	B. M.	14 6/12	135.75	14.2 over	22
66 to 67.99	B. N.	14 6/12	154.00	19.6 over	20

TABLE 23.—*Girls with Blood Pressures of 82 Systolic and 50 to 58 Diastolic and 96 Systolic and 60 to 68 Diastolic*

Size of Cuff	Blood Pressure	Range of Age, Years	Range of Weight, Pounds	Range of Height, Inches	Range of Percentage Over or Under Average Weight
Child	82/50 - 58	3 9/12 to 6 10/12	30 to 60.75	36 to 48	14 under to 17.1 over
	96/60 - 68	4 5/12 to 11 8/12	47.25 to 70.5	42 to 56	17.7 under to 22.4 over
Adult	82/50 - 58	5 1/12 to 9 9/12	45.75 to 82.75	44 to 55	16.6 under to 16.8 over
	96/60 - 68	7 4/12 to 15 8/12	51.75 to 147.5	48 to 67	14.2 under to 34.4 over

produce immediate and measurable changes in the more stable physical traits and that systolic pressure is correlated with physical development independent of age. He found blood pressures of girls to decrease after 16 years. He pointed out that blood pressures of normal children of the same age vary within wide limits. The children examined by Bogdanovitch [23] were in the recumbent position when the blood pressures were taken. The systolic pressures were found to increase more rapidly than the diastolic. Eight hundred and forty children were examined between 1925 and 1932.

Day [24] determined the blood pressures of 41 persons ranging in age from 4 months to adulthood. The auscultatory method was used. Readings were taken simultaneously with the standard infant cuff (5 cm. wide) or the child cuff (7 cm. wide) on one arm and the standard adult cuff (13 cm. wide) on the other. The arms varied in circumference from 12.5 to 32 cm. The narrower cuffs gave higher readings. Graphs on individual subjects were made of the results obtained from using varying widths of cuffs. The blood pressure was plotted against the width of the cuff. Many of the graphs showed a flattening out of the curve when wider cuffs were used. Day believed that a cuff the width of which was selected from the flattened part of the curve gave the most accurate reading. From this he concluded that a cuff should be selected as wide as would fit the arm without impinging on the elbow or the axilla.

Robinow, Hamilton, Woodbury and Volpitto [25] made direct determinations of blood pressure by use of a hypodermic manometer in the brachial artery, in most cases, on one arm while indirect determinations with the auscultatory method, with the child in the supine position, were taken on the other arm. Comparison of the results showed that the cuff used in the indirect method can be too wide. By plotting curves of blood pressures taken with cuffs of varying width, they showed that the proper width of cuff increases with the circumference and length of the arm. They stated the belief that the reason that blood pressure seems to increase with increasing age is that too wide a cuff is used on smaller children. Kerley and Lorenze [26] made determinations of blood pressure of over 1,000 children from 3 to 19 years of age seen in private

23. Bogdanovitch, V.: Arterial Pressure in Normal Serbian Children, Arch. Dis. Childhood **9**:45 (Feb.) 1934.

24. Day, R.: Blood Pressure Determination in Children: Effect of Width of Cuff, J. Pediat. **14**:148 (Feb.) 1939.

25. Robinow, M.; Hamilton, W. F.; Woodbury, R. A., and Volpitto, P. P.: Accuracy of Clinical Determination of Blood Pressure in Children with Values Under Normal and Abnormal Conditions, Am. J. Dis. Child. **58**:102 (July) 1939.

26. Kerley, C. G., and Lorenze, E. J.: Blood Pressure Observations on Children in Private Practice, J. Pediat. **20**:383 (March) 1942.

practice. They found a rather wide range of normal readings with a gradual rise in the blood pressure with increasing age. Tables 1, 2 and 3 show a summary of the results of some of these workers.

PLAN OF STUDY AND RESULTS

The purpose of the present study is to find the normal blood pressures, with the child and with the adult cuffs, for the same girls followed

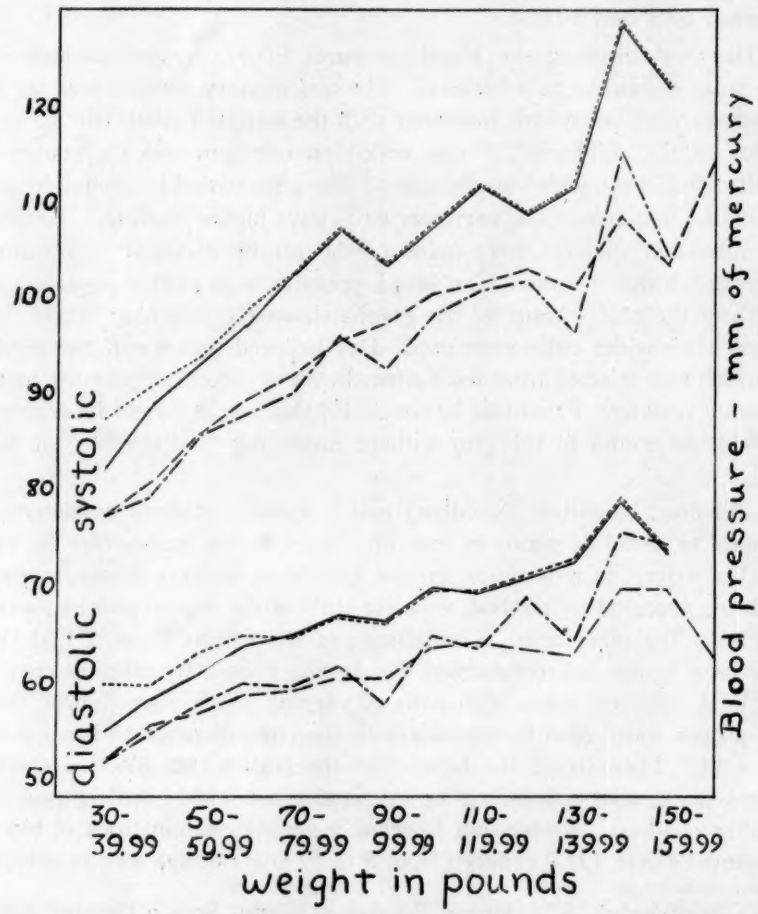

Chart 1.—Comparison between the averages of the total number of readings made with the child cuff and with the adult cuff and the averages of the readings made with the child cuff and with the adult cuff from girls in whom both cuffs were used at the same sitting. The solid line and the line of dashes represent the averages of all the readings throughout the study made when the child or the adult cuff, respectively, was used. The dotted line and the line of alternating dots and dashes represent the averages of readings made only from girls on whom both cuffs were used at the same sitting, the dotted line representing readings made with the child cuff and the line of alternating dots and dashes representing readings made with the adult cuff.

from early childhood into adolescence, and to find, if possible, the age or size at which it is best to change from the child to the adult cuff. Others have stated their views as to how the cuffs should be selected but, as far as could be determined, have not followed the same children over a period of years. In this study, blood pressures of normal, well girls in the

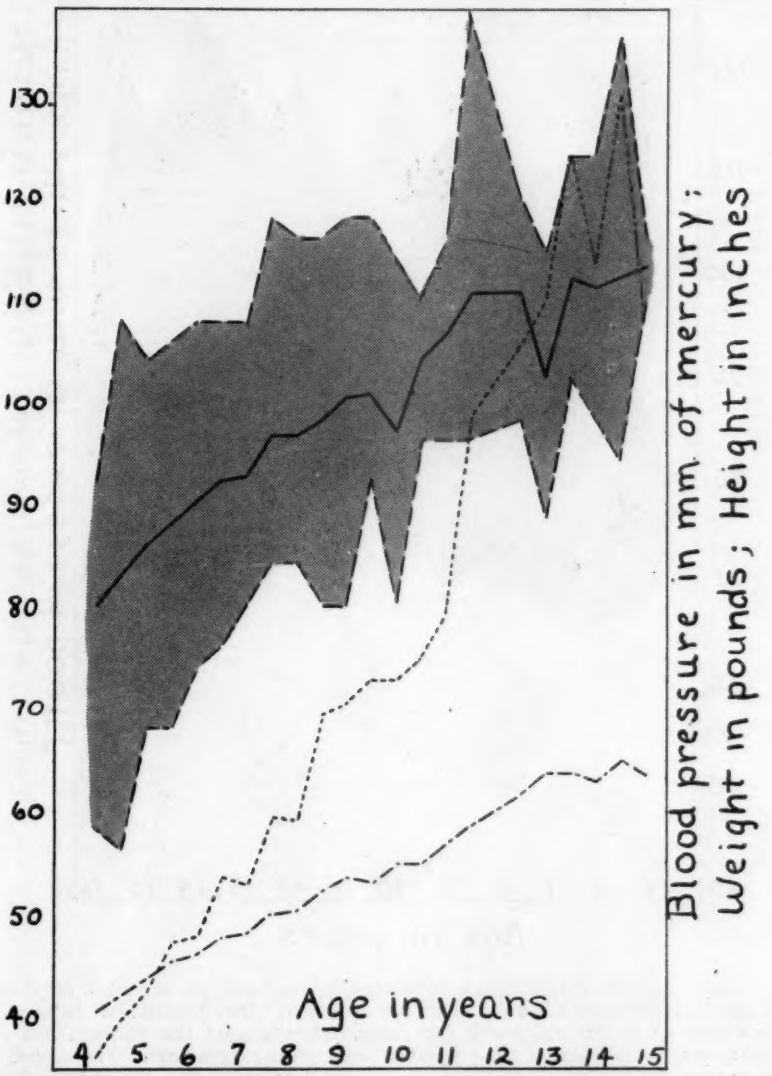

Chart 2.—Correlation between increasing age and all readings of systolic blood pressure made when the child cuff was used. The shaded area between the two lines of dashes represents the range, and the solid line through this area represents the average of these systolic blood pressure readings. The dotted line represents the average weight and the line of dots and dashes the average height at increasing age levels of all girls on whom readings were made with the child cuff.

University of Chicago Laboratory School have been taken. The youngest one to be started in the series was 3 years and 7 months old and the oldest 8½ years old. Some of those started have been removed from the series because of their having left the school. The following tabulation

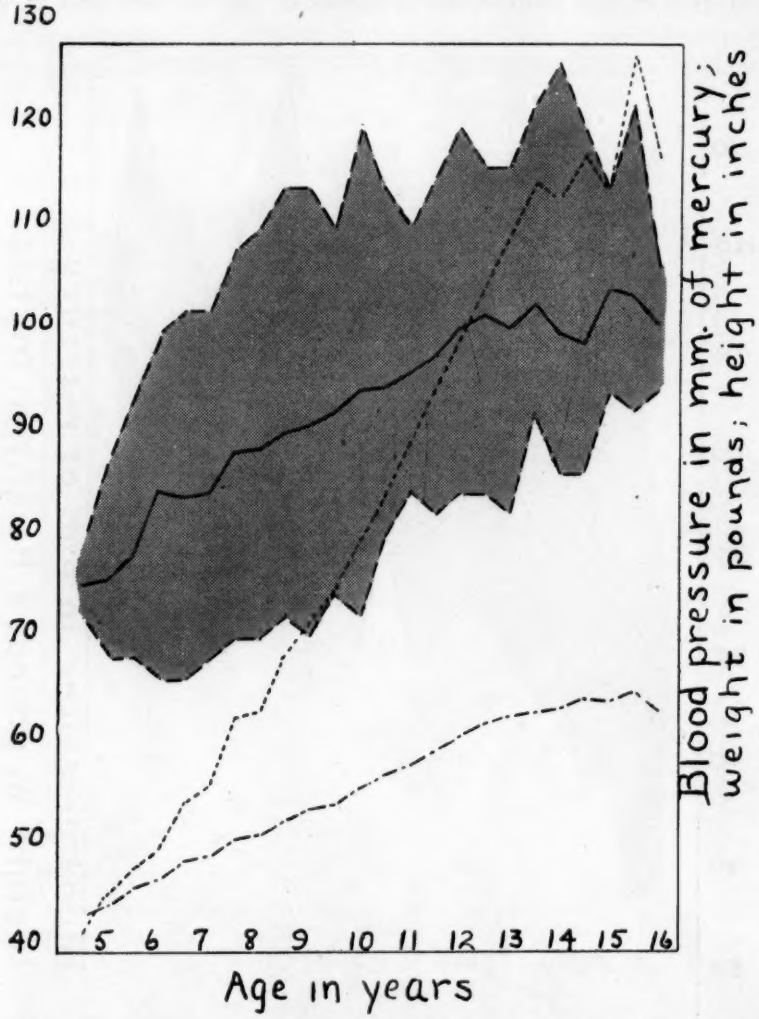

Chart 3.—Correlation between increasing age and all readings of systolic blood pressure made when the adult cuff was used. The shaded area between the two lines of dashes represents the range, and the solid line through this area represents the average of these systolic blood pressure readings. The dotted line represents the average weight and the line of dots and dashes the average height at increasing age levels of all girls on whom readings were made with the adult cuff.

shows the number of girls followed for each of a varying number of consecutive years:

No. of years followed	1	2	3	4	5	6	7	8	9	10	Total No. of Girls
No. of girls.....	10	28	35	22	23	21	15	22	31	26	233

The determinations of blood pressure were made near the end of the physical examination, when the girl had been in a lying or a sitting position for about half an hour. Girls who were new in the series were usually allowed to "play with" the apparatus for a few minutes in order to become familiar with it. Care was always taken not to pump the cuff any tighter than just above the expected systolic pressure, since a

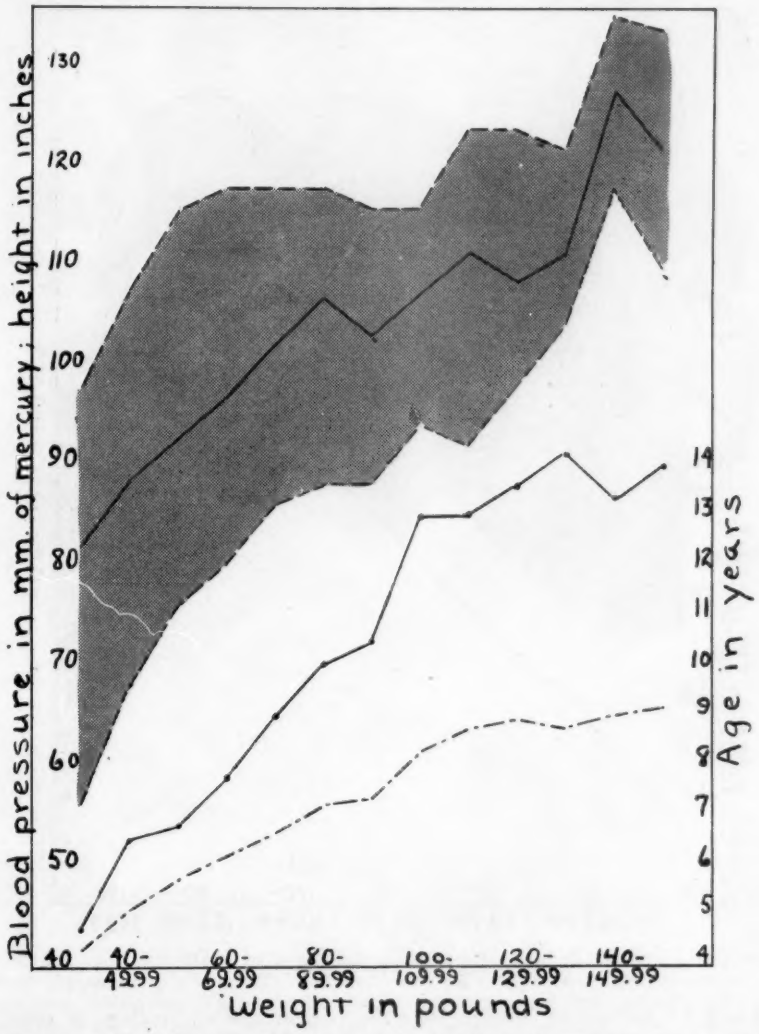

Chart 4.—Correlation between increasing weight and all readings of systolic blood pressure made when the child cuff was used. The shaded area between the two lines of dashes represents the range, and the solid line through this area represents the average of these systolic blood pressure readings. The line of alternating dots and dashes represents the average height and the line broken by small circles the average age at increasing weights of all girls on whom readings were made with the child cuff.

too tight cuff may generate fear or tensing of the muscles with a resulting inaccurate reading. Readings for girls who really seemed apprehensive were not used. Girls who were felt to be normal were included in the series even though they were known to be of a rather tense type. Readings were taken with the child in the sitting position. A Baumanometer (Riva-Rocci type of mercury manometer) was used. At the

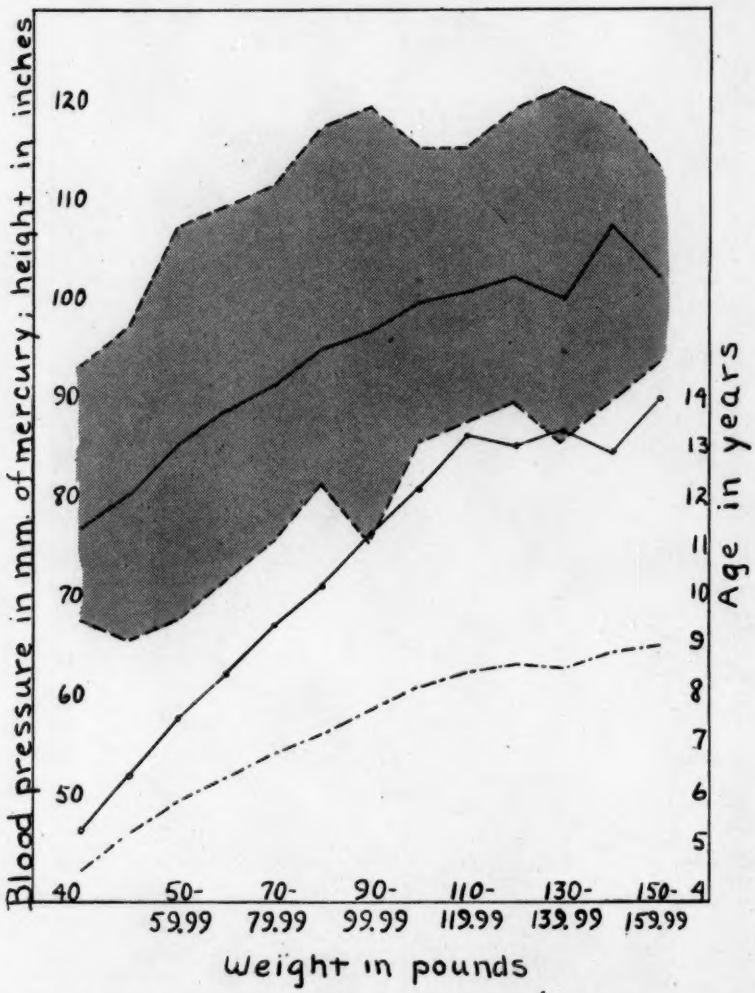

Chart 5.—Correlation between increasing weight and all readings of systolic blood pressure made when the adult cuff was used. The shaded area between the two lines of dashes represents the range, and the solid line through this area represents the average of these systolic blood pressure readings. The line of alternating dots and dashes represents the average height and the line broken by small circles the average age at increasing weights of all girls on whom readings were made with the adult cuff.

beginning of the study in 1936 either the standard child size cuff (9.5 cm. wide) or the standard adult size (13 cm. wide) was used—whichever seemed to fit best. Later, on some girls, both cuffs were used, one

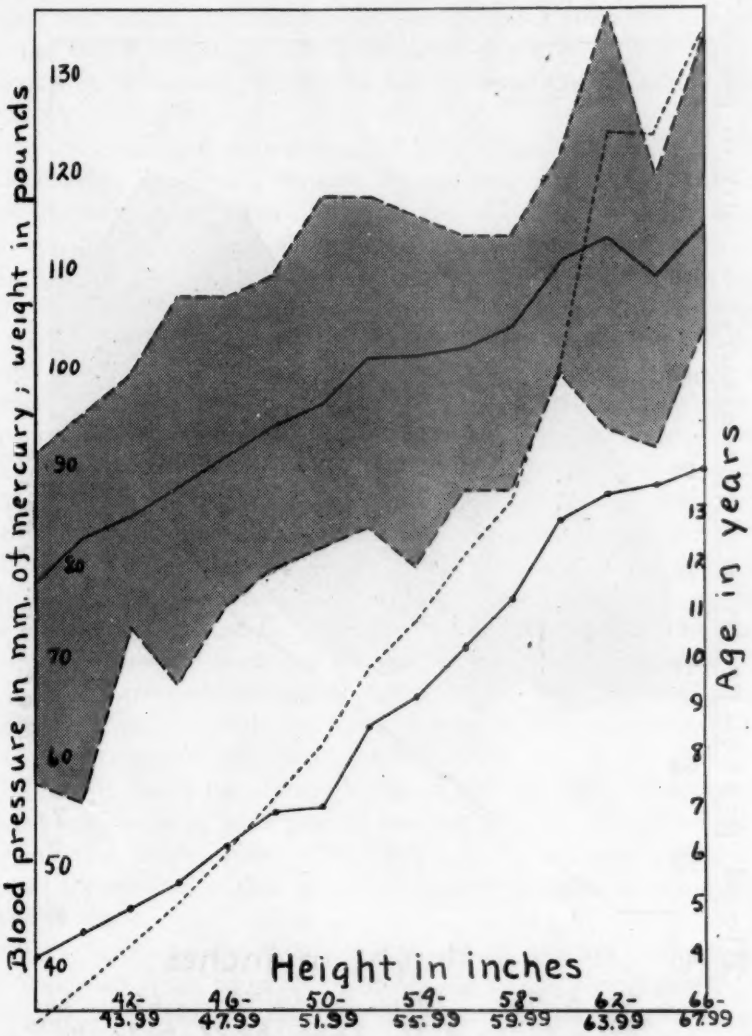

Chart 6.—Correlation between increasing height and all readings of systolic blood pressure made when the child cuff was used. The shaded area between the two lines of dashes represents the range, and the solid line through this area represents the average of these systolic blood pressure readings. The line of dots represents the average weight and the line broken by small circles the average age at increasing heights of all girls on whom readings were made with the child cuff.

immediately after the other. Pressures were determined by the auscultatory method with the bell of the stethoscope at the bend of the elbow.

The systolic pressure was counted as the point at which the first pulse beat was heard as the pressure was decreased, and the diastolic as the point at which there was a rather sudden fading of the sound just before it disappeared completely.

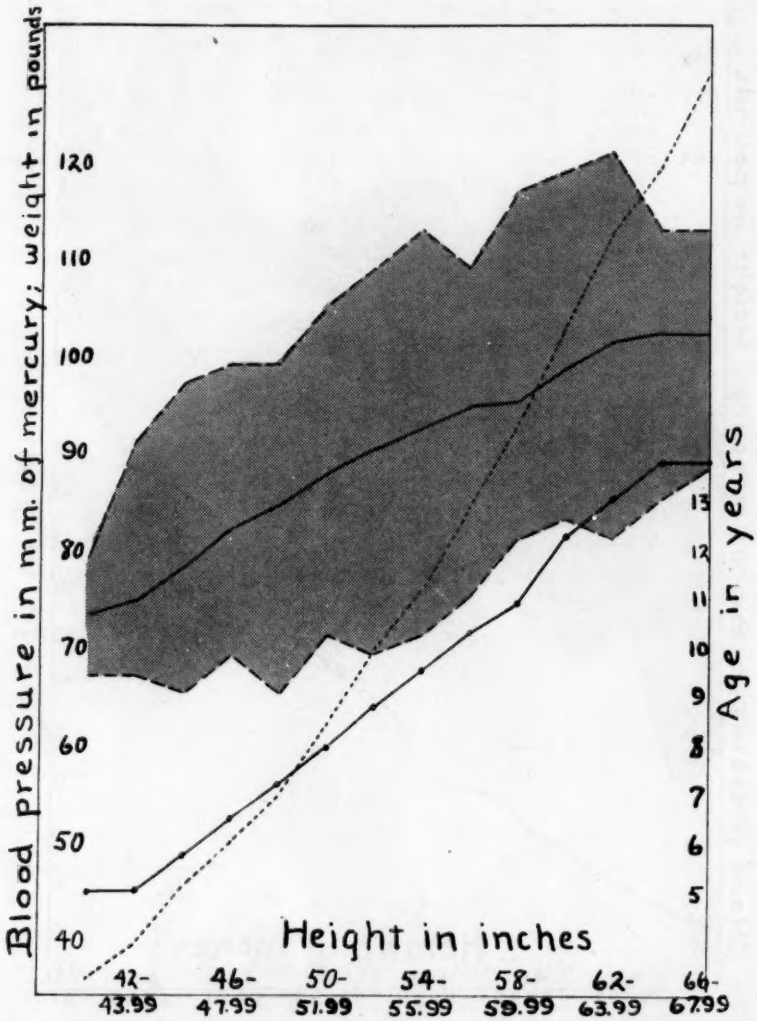

Chart 7.—Correlation between increasing height and all readings of systolic blood pressure made when the adult cuff was used. The shaded area between the two lines of dashes represents the range, and the solid line through this area represents the average of these systolic blood pressure readings. The line of dots represents the average weight and the line broken by small circles the average age at increasing heights of all girls on whom readings were made with the adult cuff.

Tables 4 through 6 show the records of individual girls followed for various numbers of years. Tables 7 through 18 show the ranges and

averages of the readings for all girls divided according to increasing ages, increasing weights and increasing heights. Tables 19 and 20 show ranges and averages according to increasing weights for only those girls on whom both cuffs were used at the same sitting. On all tables, overweight and underweight are calculated from the standards on the weight-height-age tables prepared by Bird T. Baldwin and Thomas D. Wood and published by the American Child Health Association.

In the charts are plotted some of these ranges and averages. The shaded areas in charts 2 through 7 show the ranges; the solid lines through these areas show the averages. Chart 1 is a comparison between the averages of all the readings made when the child cuff was used and all the readings made when the adult cuff was used with those from girls on whom both cuffs were used at the same sitting. It shows that the results are much the same even though the two cuffs were not used on the same girl at the same time. It brings out a slightly greater difference between the child and adult readings which may be accounted for partly on the basis of the smaller number of cases.

In the tables showing records of individual girls, C.A. is an unusually "normal" girl in build and temperament; C.B. is a small, wiry, active girl; C.C. always has been tall for her age but well developed; C.D. is of a rather heavy build, and C.G. is a well proportioned girl but always has been small for her age. It is interesting to compare the records of C.B. and C.D. who are the opposite in build but whose blood pressures run much the same. C.C. and A.U. are both tall, but A.U. is of a more slender build. C.O. and C.P. have remained almost alike in age, weight, height and blood pressure through six years, though C.P. appears to be a more tense type than C.O.

Table 21 shows the averages of blood pressures for girls more than 10 per cent under or more than 15 per cent over the average weight, at the different height levels. The differences do not seem sufficient to justify the conclusion that weight is overly important in determining blood pressure.

The slightly greater increase in the blood pressure readings with the child cuff at the 52 to 53.99 inch (132.1 to 137.1 cm.) height level over the 50 to 51.99 (127 to 132.1 cm.) inch level in table 17 may indicate that this is the best point at which to change from the child to the adult cuff. Table 22 shows the girls with the greatest and least differences between the readings with the child and with the adult cuff when both cuffs were used at the same sitting. The fact that there are more girls at the 50 to 51.99 inch and 52 to 53.99 inch periods with no difference between the readings and that the differences increase beyond this height may be another indication that this is the best point at which to change from the child to the adult cuff.

Judson and Nicholson [14] stated that blood pressure depends on four factors: the force and rate of the heart beat, the peripheral resistance, the elasticity of the walls of the blood vessels and the character of the blood, such as volume and viscosity. It is known that various conditions can affect these factors. For table 23 all girls having a blood pressure arbitrarily chosen at 82 mm. of mercury systolic and 50 to 58 mm. diastolic and all girls having a blood pressure arbitrarily chosen at 96 mm. of mercury systolic and 60 to 68 mm. diastolic were selected. The wide range of age, weight, height and percentage overweight or underweight shows that a variety of factors must combine to produce the same blood pressures.

CONCLUSIONS

Blood pressure in a single child may vary considerably from day to day. The increase in blood pressure in a subject is not constant from year to year. There may even be a decrease from one year to the next. Each child has his own pattern. Many factors may affect this pattern, making a wide range for the so-called normal. The important thing from the clinical viewpoint is to know the normal range of blood pressure with the width of cuff used for the given age and size of child in question and to know when the child varies from his own normal or gets out of the normal range for his size. The adult cuff does not fit all adults in the same way. If on the child the cuff is used which is about the same width in proportion to the size of his arm as the adult cuff is to the size of the average adult arm, the readings probably are comparable.

ALEXANDER'S RABBIT SERUM IN THE TREATMENT OF INFLUENZAL MENINGITIS

An Evaluation of Its Use in Conjunction with Sulfonamide Compounds

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MENINGITIS, particularly that caused by Hemophilus influenzae type B, presents an emergency greater than does acute appendicitis because an inadequacy in treatment usually results in permanent injury or death. The fate of the child with influenzal meningitis hinges so completely on the promptness and intensity of treatment that presentation of further data on both chemotherapy and Alexander's anti-influenzal rabbit serum seems justified.

The need for impressing physicians with this fact is presented in the following series of 47 patients admitted to the Milwaukee Children's Hospital from January 1939 to April 1946, which is the span of time since Alexander's serum has been available and sulfonamide compounds have been given in massive dosages. Previous to this time, from 1923 to 1939, there had been admitted to this hospital 66 patients with proved influenzal meningitis who were treated with a great variety of ineffective methods. All but 3 died, a mortality rate of 95 per cent!

As indicated later in this article, results in the treatment with sulfonamide compounds alone have not been too successful, but results with adequate amounts of serum and sulfonamide compounds together were excellent. We have not, however, always been able to sterilize the spinal fluid, even with large doses of serum and sulfonamide drugs. The virulence of the organisms, the route of administration, the unpredictable complications or sequelae and the possibility of sulfonamide-resistant organisms all influenced these results. Lack of adequate dosages of the serum and delay in starting treatment were unquestionably the cause of many of the adverse results.

These cases were managed by several physicians, pediatricians as well as general practitioners, with varying individual standards of treatment. In some instances an adequate amount of serum was not available. A study of the results indicates the urgent and vital need of diagnostic spinal punctures on the least suspicion of meningitis and

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also points to the need for recognized minimal standards of treatment. Buchanan has said that to wait for the usually accepted signs and symptoms of meningitis before doing a puncture on an infant is wrong almost every time because the puncture should have been done sooner.[1]

It is not within the scope of this paper to discuss the signs and symptoms of this disease or its complications and sequelae. It deals only with the treatment in so far as life-saving measures are concerned.

The cases in this report follow rather closely the groupings of other authors' cases.[2] The incidence of the onset of the disease was highest in October and November and lowest in August and September, as indicated in chart 1.

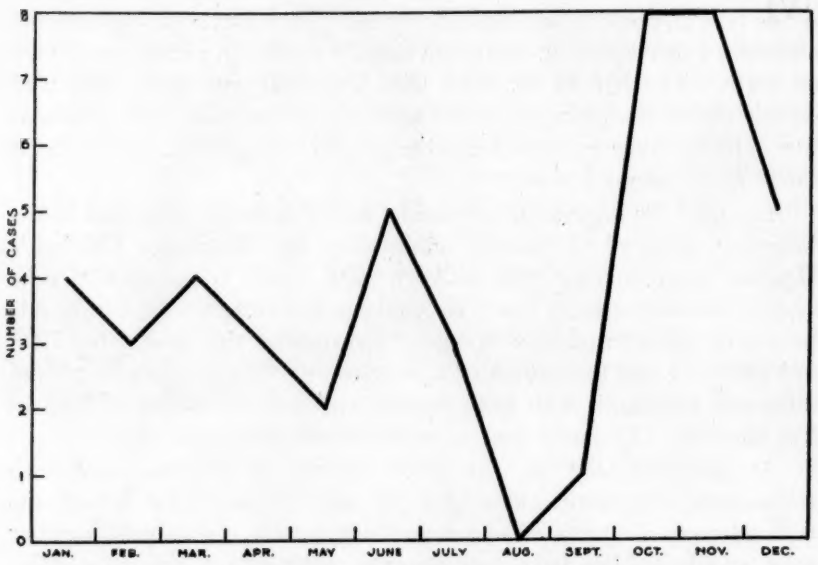

Chart 1.—Onset of symptoms in influenzal meningitis, by month.

The ratio between boys and girls was 1.5. Charts 2 and 3 indicate that 85 per cent of the children who had this disease were 2 years old or younger; 73 per cent of the children under 12 months of age succumbed, and 79 per cent of the recoveries occurred in children over 12 months of age!

In the 47 cases being reported on, 21 patients recovered, 2 were unimproved (they were taken home against advice, and therefore no evaluation of the efficacy of the treatment could be made) and 24 died—an over-all mortality rate of 51 per cent. Nine of the patients who died

1. Buchanan, D. N.: Personal communication to the authors.

2. Smith, M. H. D.; Wilson, P. E., and Hodes, H. L.: The Treatment of Influenzal Meningitis, J. A. M. A. **130**:331-335 (Feb. 9) 1946.

were in the hospital twenty-seven hours or less, and since treatment of patients with so severe a disease could not be adequate in this short period of time, they are not included in the evaluation of the therapy given. If these cases are excluded, the mortality rate is reduced to a corrected figure of 39.4 per cent. Of the remaining 15 children who

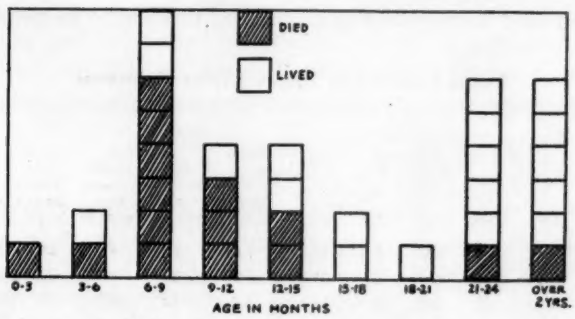

Chart 2.—Ratio of children who died and those who lived, by age groups.

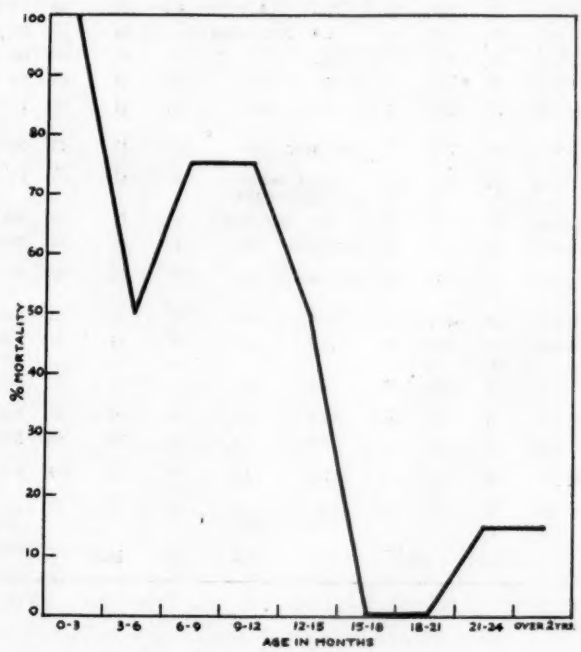

Chart 3.—Mortality rate, by age groups.

succumbed to the disease, only 3 received adequate serum and sulfonamide therapy according to Alexander's standards.[3] The mortality rate

3. Alexander, H. E.; Ellis, C., and Leidy, G.: Treatment of Type Specific Hemophilus Influenzae Infections in Infancy and Childhood, J. Pediat. **20**:673-698 (June) 1942.

is reduced, then, to 12.5 per cent when currently accepted dosages are used in patients who are not moribund. Tables are presented to substantiate these figures.

From the charts the following conclusions can be drawn:

1. Of the 9 patients who were treated with sulfonamide compounds alone, 7 died and 2 lived. The average sulfonamide levels of the patients who died were even higher than of those who recovered (aver-

TABLE 1.—*Data on Patients Who Recovered*

Year	Case	Age	Sex	Total Amount Serum, Mg. I.V.*	Total Amount Serum, Mg. I.T.†	Sulfonamide Levels Blood	Sulfonamide Levels Spinal Fluid	Sugar in Spinal Fluid Admission	Sugar in Spinal Fluid Discharge	Hospital Days	Sequelae
1946	1	3 yr.	M	200	0	10.1	7.45	20	42	58	No residual
	2	2 yr.	M	150	0	14.4	5.2	21	49	30	No residual
	3	8 mo.	M	100	0	12.5	4.3	12	51	68	Hypotonicity of muscles
1945	1	22 mo.	M	125	0	7.9	4.0	33	40	22	No residual
	2	4 mo.	F	100	0	23.5	4.15	4.5	43	60	No residual
	3	2 yr.	F	50	0	8.9	Not taken	31	54	23	No residual
	4	2 yr.	F	175	75	25.1	7.9	0	47	47	No residual
	5	5 yr.	M	150	0	15.5	12.4	14.5	48	69	No residual
	6	23 mo.	M	150	0	7.2	6.9	5	44	55	Increased intracranial pressure
	7	2 yr.	F	100	0	Not taken	2.8	25	41	15	No residual
1944	1	11 mo.	M	100	0	1½ gr. per lb. body weight		39	45	30	No residual
	2	15 mo.	F	350	0	6.7	Not taken	6	42	25	No residual
	3	20 mo.	M	75	0	Not taken	6.4	4	36	45	No residual
1943	1	6½ mo.	F	100	0	Not taken	6.5	30	48	47	Spastic left arm and leg
	2	3 yr.	M	100	0	20.3	6.2	30	48	26	No residual
	3	16 mo.	F	125	0	11.2	5.5	12	49	21	? Hemiatrophy of brain
	4	13 mo.	F	125	0	4.8	5.3	10	58	15	No residual
1942	1	5½ yr.	M	25	50	11.8	6.5	28	59	23	No residual
	2	17 mo.	F	50	25	10.5	6.4	25	76	95	No residual
1940	1	2½ yr.	M	0	0	5.8	5.0	8	71	129	No residual
1939	1	2½ yr.	F	0	0	1½ gr. per lb. body weight		15	45	87	Equilibrium disturbed
Averages.....				132.0		12.2	6.0	17.7	49.3		

* I.V.: intravenously.
† I.T.: intrathecally.

age level in the blood of 18, compared to a level of 12.2; and average level in spinal fluid of 11.2 as compared to a level of 6.0). Of course these levels do not represent a true index of the adequacy of administration of sulfonamide drugs, and too much significance should not be attached to them for the following reasons: (1) Some sulfonamide levels were determined after administration of dextrose; (2) there

may have been an increase or decrease in the level between readings; (3) in some cases the level was determined only once; (4) the levels in the blood and in the spinal fluid were not always determined at the same time; (5) in some cases the levels were not determined at all, and (6) in almost all cases the levels were not determined at consistent intervals. Most of the sulfonamide compounds given were in dosages of 1½ grains per pound (216 mg. per kilogram) of body weight per

TABLE 2.—*Data on Patients Who Died*

Year	Case	Age	Sex	Total Amount Serum, Mg. I.V.*	Total Amount Serum, Mg. I.T.†	Sulfonamide Levels Blood	Sulfonamide Levels Spinal Fluid	Sugar in Spinal Fluid on Admission	Hospital Days	Comment
1946	1	12 mo.	M	75	0	44.4	40.0	12	8	Only 1 dose of serum given
1945	1	10 mo.	M	125	25	7.7	12.6	32	59	Abscess of brain developed
	2	8 mo.	F	150	0	62.0	Not taken	29	7	Serum given in 2 doses
1944	1	8 mo.	M	0	0	1½ gr. per lb. body weight		7	20	No serum given
1943	1	10 mo.	M	0	0	17.6	Not taken	6	17	No serum available
	2	7 mo.	M	100	0	9.7	8.2	8	37	Initial dose of serum small
	3	5½ mo.	M	100	0	6.2	13.9	3.5	24	Diagnosis delayed 10 days; pleural effusion
1942	1	8½ mo.	M	25	50	11.8	5.1	5	39	Initial dose of serum small
	2	14 mo.	M	0	0	Not taken	9.3	6	35	No serum given
	3	23 mo.	M	0	0	12.4	8.4	7	19	Diagnosis delayed 11 days
	4	2 mo.	M	25	0	11.6	7.4	9	11	Serum not available for 6 days after diagnosis was made
1940	1	7½ mo.	F	50	25	10.3	3.2	8	19	Diagnosis delayed 7 days
	2	13 mo.	F	0	0	4.6	4.2	4	28	No serum given
1939	1	2½ yr.	M	0	0	1 gr. per lb. body weight		Not done	29	No serum given
	2	8 mo.	F	0	0	1½ gr. per lb. body weight		0	10	No serum given
Averages.....				93.5		18.0	11.2	9.7		

* I.V.: intravenously.
† I.T.: intrathecally.

day, which is considered adequate or excessive in most diseases. However, in meningitis we believe that initially the patient should receive approximately 3 grains per pound (431 mg. per kilogram) per day; this high level should be maintained with approximately 2 grains per pound (287 mg. per kilogram) per day during the acute infection. In order to establish a high level rapidly the first dose should be given intravenously as the sodium salt of the sulfonamide drug, and subsequent doses should be given subcutaneously or intravenously if the patient is not able to receive and retain the oral medications.

It cannot be stressed to strongly that unless alkalis are given in proportionate amounts, sulfonamide crystals and red blood cells will appear in the urine. It is our policy not to decrease the sulfonamide intake if only crystals are found in the urine; however, we either decrease or stop the administration of sulfonamide drugs when appreciable hematuria occurs. If sulfonamide crystals alone are present, then alkalis are increased and administration of the drug is continued. In most cases of mild hematuria the urine clears in a few days, and sulfonamide compounds are cautiously readministered.

2. The average amount of sugar in the spinal fluid was lower on admission in those patients who died than in those who survived the infection (9.7 mg. per hundred cubic centimeters as compared to 17.7). Six of the patients who survived, however, had less than 10 mg. per hundred cubic centimeters. It is interesting to note that 1 of the patients who survived with only sulfonamide therapy had at the time of his admission only 8 mg. of sugar in the spinal fluid per hundred cubic centimeters, and that 1 of the patients who survived with serum and sulfonamide therapy combined had no sugar in the spinal fluid at the time of his admission. Can significance be attached to the initial sugar content of the spinal fluid as an index of the virulence of the organism? It might mean that in the cases in which the level was low the disease was more fulminating than in those in which the level was higher; on the other hand, serum was not administered in 7 of these cases, and in only 2 of them was the presently recommended initial dose of serum given.

3. The average amount of serum administered was higher for those patients who survived than for those who died (132 mg. as compared to 93.5 mg.). There were 8 patients who received serum but did not survive the infection. Of these, 3 did not receive the recommended initial dose of rabbit serum; 1 was not given serum until ten days after admission, and it is believed that he had meningitis as part of his illness most of this time; in the other case, the initial serum therapy was not followed by subsequent dosages.

4. No attempt will be made to evaluate the efficacy of intrathecal injections. In the few cases, 6, in which serum was given in this manner, no untoward or beneficial effects were determinable (3 patients died and 3 recovered).

DISCREPANCIES IN MANAGEMENT AND TREATMENT

1. *Delayed Diagnosis.*—There were 2 cases in which a diagnosis of pneumonia with pleural effusion was made, but the possible presence of an accompanying meningitis was not considered. In reviewing these charts one can see by the histories that meningeal symptoms were

present prior to the patients' admission but were not thought to be significant in view of the presence of pleural effusion. In these cases the diagnosis of meningitis was delayed ten and eleven days, during which time the meningitis was culminating. In children under 1 year of age the Kernig and Brudzinski signs are late manifestations of the disease, and the question of voluntary muscular spasm versus involuntary spasm is always present. The earliest sign of meningitis is the tenseness of the fontanel, which is often interpreted as a result of crying and irritability in a child during the examination. The fontanel must be reexamined when the child is quiet before judgment can be passed. The tenseness of the fontanel plus the history of vomiting, and the irritability of the child when handled, should always be investigated by means of a spinal puncture. It is much better to obtain normal fluid in large series of cases than to miss abnormal fluid in 1 case. The contraindications for a spinal puncture are so few and the hazards so slight that the procedure should be used more routinely. With careful technic and usual precautions, no harm should come to the child. One of the patients had vomited before admission and had had a cold, fever, cough and moaning cry during the previous week. This, plus a peculiar listlessness, suggests in retrospect meningitis, but because the child had definite pneumonia with pleural effusion, this diagnosis was not considered. The second patient who was admitted with the diagnosis of pleural effusion was rather irritable when picked up and handled, and looked apprehensive. The nurse reported on the first night that the child was "stiff" at times. Here again, in retrospect, the possibility of meningitis might have been entertained. The presence of the disease of the chest capable of producing meningeal irritation was disarming. It is interesting to note in passing that both these patients had icterus. As can be seen from the chart of deceased patients all but 1 of the children who died were under 2 years of age. The absence of classical signs and symptoms with delayed diagnosis in this young group surely was contributory to the high mortality rate.

2. *Failure to Follow the Initial Dose of Serum with Studies Designed to Determine the Adequacy of Treatment.*—This also contributed to the mortality rate in the reported cases. The child may have been given the initial dose as recommended by Alexander in accordance with the levels of sugar in the spinal fluid determined, but this was not always followed by the test of capsular swelling, and no more serum was given. From the response in those patients in whom follow-up tests and serum were given, it is believed that some of these patients might have lived had they been treated according to the standards recommended by Dr. Alexander.

3. *Lack of Sufficient Intravenous Fluids Prior to the Administration of the Serum.*—Alexander states that the intravenous fluids tend to

decrease the amount of free type-specific carbohydrate in the blood stream by eliminating it via the kidneys. This allows the serum to combat the carbohydrate in the capsule of the organism instead of expending itself on that already liberated. Most of these patients are dehydrated, too, and intravenous fluids will combat this deficiency.

4. *Complete Trust in the Oral Route of Administration of Sulfonamide Drugs.*—Oral, instead of intravenous or subcutaneous, administration undoubtedly contributed to the mortality rate. The nurse could state definitely that all the medicament was given but could not state how much of it might have been expectorated or regurgitated by the patient. The primary dose, as stated previously, should always be given intravenously as the sodium salt of the sulfonamide drug. The levels in the blood and the spinal fluid should be checked at consistent intervals, because doses which are necessary to maintain desired levels vary greatly.

Sequelae appeared in 5 of the 21 cases in which there was recovery, in 1 of which there was sulfonamide therapy without administration of serum. One girl, aged 7½ years, lost her sense of equilibrium and became unsteady on her feet; 1 girl, 6½ months of age, had a spastic arm and leg on discharge; 1 boy, 23 months old, possibly had hydrocephalus on discharge but at the present time shows no evidence of any increased intracranial pressure; 1 girl, 16 months of age, came back to the hospital three years later with hemiatrophy of the brain, and 1 boy, 1 month of age, left the hospital with some hypotonicity of his muscular system but at present is developing normally.

SUMMARY AND CONCLUSIONS

From January 1939 to the present time, April 1946, 47 patients with influenzal meningitis were admitted to the Milwaukee Children's Hospital. Two were unimproved (taken home against advice), 24 died and 21 recovered. Nine of the 24 patients who died were hospitalized twenty-seven hours or less and could not be considered in judging the usefulness of immune rabbit serum therapy in conjunction with administration of sulfonamide drugs. Eight patients died who were given both serum and sulfonamide drugs. Only 3 of these received what we now believe to be adequate serum therapy. The mortality rate in patients with influenzal meningitis who were adequately treated with sulfonamide drugs and Alexander's serum, therefore, was 13.6 per cent (patients treated only with sulfonamide drugs are eliminated). Twenty-two patients were treated adequately according to Alexander's standards; 19 recovered and 3 died.

Nine patients were treated with sulfonamide drugs and without serum therapy. Two lived and 7 died, a mortality rate of 77 per cent.

Diagnosis of influenzal meningitis must be made early in order to combat it effectively with rabbit serum and sulfonamide drugs.

Sulfonamide drugs must be given in high concentrations and must be given by intravenous or subcutaneous routes in order to assure correct dosages.

Serum should be preceded by intravenous fluids so that the free floating type-specific carbohydrate of the organism is eliminated from the blood stream and the dehydration alleviated.

Initial serum therapy must be followed by additional serum as indicated by the level of sugar in the spinal fluid and culture and capsular swellings of the organisms with the patient's serum.

Alexander's anti-influenzal rabbit serum (administered according to her recommendations) combined with sulfonamide drugs is 85 per cent efficient in those cases in which therapy is instituted before the patient is moribund. To date it is the only efficient method for treating meningitis due to Hemophilus influenzae type B.

Case Reports

XANTHOMA TUBEROSUM, AORTIC STENOSIS, CORONARY SCLEROSIS AND ANGINA PECTORIS

Report of a Case in a Boy Thirteen Years of Age

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DISEASE of the coronary arteries alone or with angina pectoris is rarely found in children. For that reason it is thought of interest and importance to report the case of a boy 13 years of age who had xanthoma tuberosum, a typical history of angina pectoris and significant changes in the electrocardiogram, and to review similar cases from the literature.

REPORT OF A CASE

The patient, a boy 13 years old, was first seen at the Mayo Clinic on Aug. 22, 1945. Seven years previously soft, fluctuant, yellowish pink, circumscribed tumors had begun to develop on the elbows, knees, ankles, joints of the fingers and toes and the buttocks. On two occasions similar lesions had been removed surgically from the heel and knee, and they had been reported to contain white material "like cottage cheese." The masses had never been tender. For six to eight months before admission the patient had had dyspnea and substernal pain on exertion. Walking one block produced this pain, and it was relieved by rest. No attack lasted more than five minutes, and no history of rheumatic fever was given. Neither familial xanthomatosis nor heart disease was present in the patient's family.

On physical examination at the Clinic the lesions of xanthoma tuberosum mentioned in the history were found (figs. 1 and 2). On examination of the heart a systolic murmur was heard over the precordium; it was loudest over the aortic area. This murmur was transmitted to the large vessels of the neck and was heard on the back. It was thought that the aortic systolic murmur was due to aortic stenosis and that the aortic stenosis was in turn due to xanthomatous infiltration of the aorta and aortic valves. Blood pressure on two occasions was 132 and 148 mm. of mercury systolic and 84 and 70 mm. diastolic, and the pulse rate was 104 beats per minute. Examination gave otherwise negative results.

Laboratory Data.—The urine was normal except for occasional erythrocytes. The amount of hemoglobin was 13.1 Gm. per hundred cubic centimeters of blood. No abnormality was revealed by serologic examination. The concentration of all the fat components of the plasma was increased: the value for cholesterol was 561 mg. per hundred cubic centimeters; cholesterol esters, 360 mg.; total

From the Division of Medicine, Mayo Clinic.

fatty acids, 948 mg., and total lipoids, 1,509 mg. The level of lecithin in the blood was 496 mg. per hundred cubic centimeters. By the Westergren method, the sedimentation rate was 43 mm. per hour.

A roentgenogram of the head showed calcification of the internal carotid arteries on both sides of the sella turcica. Roentgenograms of the legs and feet showed swelling of the soft tissue of both feet and anterior to the right and left knees. The bones showed no abnormalities. Roentgenographic examination of the chest revealed nothing significant.

The electrocardiogram, taken when the patient was at rest (fig. 3), revealed a rate of 86 with isoelectric T waves in lead II and inverted T waves in leads III, IV R and IV F. It was believed that these abnormalities were due to xanthomatous involvement of the coronary arteries. To confirm this impression it was decided to do an anoxia test. The boy was sent to the electrocardiographic laboratory for this test. He previously had undergone an operation for which he had been given gas anesthesia. On seeing the oxygen tank he became extremely frightened and began to cry, as he thought he was going to have another operation.

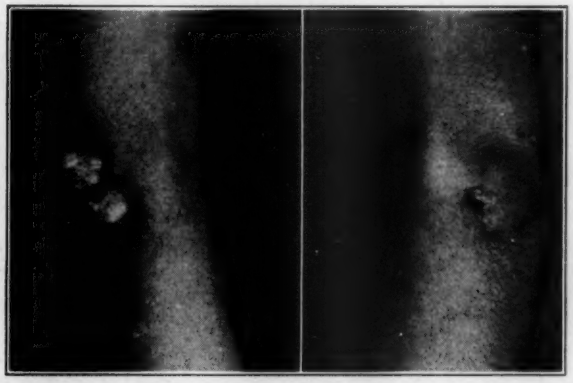

Fig. 1.—Circumscribed lesions of xanthoma tuberosum on elbows.

Suddenly he experienced a severe substernal pain which extended down both arms. An electrocardiogram taken during this attack (fig. 3) revealed a rate of 129, considerable depression of the S-T segments in leads I and II and even more depression of the S-T segments in leads IV R and IV F. Because of his severe pain it was thought inadvisable to do the anoxia test and the changes in the electrocardiogram taken during the attack of pain were considered the same as those that would have been obtained if the test had been carried out.

COMMENT

According to Thannhauser's classification,[1] primary xanthomatosis may be divided into two subgroups: the hypercholesteremic and the normocholesteremic type. In the hypercholesteremic type xanthoma of the tendons and tendon sheaths, xanthoma tuberosum and xanthoma planum of the skin, xanthomatosis of the bile

1. Thannhauser, S. J., and Magendantz, H.: The Different Clinical Groups of Xanthomatous Diseases: A Clinical Physiological Study of Twenty-Two Cases, Ann. Int. Med. **11**:1662-1746 (March) 1938.

ducts with secondary jaundice and biliary cirrhosis, cardiovascular involvement and scattered nests of xanthoma cells in the spleen, liver and lymph nodes occur. In the normocholesteremic type xanthoma disseminatum of the skin, mouth and larynx, osseous involvement of the skull, scapula, pelvis, extremities and orbits, xanthomatous involvement of the pituitary gland and tubercle of Rolando (tuber

Fig. 2.—Lesions of xanthoma tuberosum on feet; *a*, anterior view; *b*, posterior view.

cinereum) with diabetes insipidus and also involvement of the brain, medulla and dura, involvement of the lungs and pleura and scattered nests of xanthoma cells in the spleen, liver and lymph nodes as in the hypercholesteremic type occur. Three cases have been reported which have features of both subgroups, according to Thannhauser's reveiw. The case presented in this paper is typical of the

hypercholesteremic type because of the cardiac involvement and xanthoma tuberosum of the skin and xanthoma of the tendons.

Little is known definitely concerning the causation of primary xanthomatosis. Thannhauser suggested that it is a disease of reticular cells caused by intracellular disorder of cholesterol metabolism.

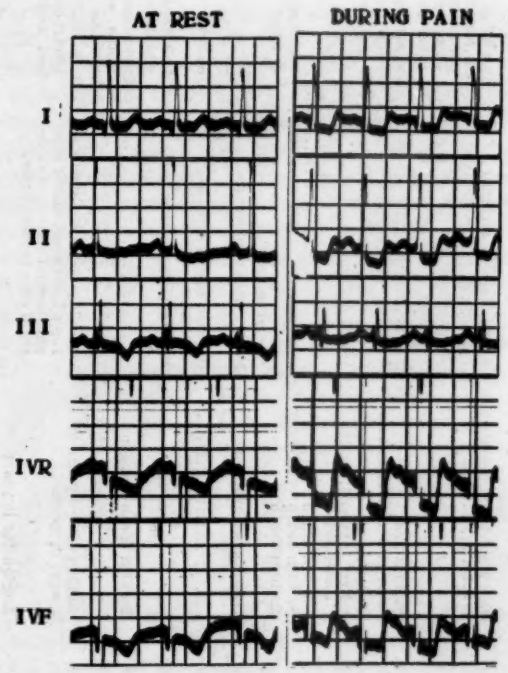

Fig. 3.—The electrocardiogram taken at rest shows a rate of 86, isoelectric T waves in lead II and inverted T waves in leads III, IV R and IV F. The electrocardiogram taken during the attack of severe pain reveals a rate of 129, depression of the S-T segment in leads I and II and pronounced depression of the S-T segment in leads IV R and IV F.

TABLE 1.—*Six Youngest Patients Who Had Xanthoma Tuberosum with Hyperlipemia Seen at the Clinic*

Age at Onset, Years	Age, Years *	Secondary Lesions or Type of Death	Comment
16	39	Angina pectoris	
12	19	None	
22	31	Sudden cardiac death	
2	15	None	Familial xanthomatosis
5	5½	None	Patient had nephrosis

* Age at last examination or at time secondary lesion developed.

From the records at the Mayo Clinic, in which only 27 cases of xanthoma tuberosum with hyperlipemia have been found to date, it can be concluded that the disease is rare among both adults and children. The ages of the 6 youngest patients at the onset of symptoms ranged from 2 to 22 years (table 1).

TABLE 2.—*Summary of Reported Cases of Xanthoma Tuberosum and Associated Heart Disease in Children and Adults Who Were Twenty-Three Years or Less at Onset of Cardiovascular Lesion*

Date	Author	Age (Years) and Sex	Symptoms and Signs or Type of Death	Cardiac Lesion or Sign	Comment
1879	Fox [5]	21 F	Angina; dyspnea	Loud mitral diastolic murmur	Rheumatic heart disease (?)
1883	Poensgen, A.: Virchows Arch. f. path. Anat. **91**: 350-370, 1883	12 M	.....	Aortic stenosis	
1889	Lehzen, G., and Knauss, K.: Virchows Arch. f. path. Anat. **116**: 85-104, 1889	11 F	Sudden death, typical of coronary disease	Mitral diastolic murmur	Extensive xanthomatous plaques in aorta, large arteries and coronary arteries and mitral valve; had sister with xanthoma tuberosum
1905	Gwynne, C. N.: Rep. Soc. Study Dis. Child. **5**: 318-322, 1905	10 M	Sudden death	Mitral murmur	No necropsy
		10 M	.....	Mitral systolic murmur	Sibling of previous patient
1910	Low, R. C.: Brit. J. Dermat. **22**: 100-118, 1910	11 F	Fainting and giddiness; liver enlarged; veins distended	Loud systolic beat heard over aortic area	No necropsy
1910	Arning [3]	16	Sudden death	.....	Siblings; 2 died while dancing
		21	Sudden death	.....	
		26	Sudden death	.....	
		16	.....	"Heart lesions"	
1921	Knowles, F. C., and Fisher, H. N.: J. A. M. A. **77**: 1557-1560, 1921	10 M	Dyspnea on exertion	Loud systolic murmur	
1925	Lapowski: Arch. Dermat. & Syph. **11**: 701-702, 1925	8 F	.....	Blowing apical systolic murmur	Cholesterol, 315 mg. per cent
		7 F	.....	Mild systolic murmur	Cholesterol, 325 mg. per cent; sibling of previous patient
1934	Hess, F. O.: München. med. Wehnschr. **81**: 579-580, 1934	19 F	Sudden death (cardiac)	.....	Xanthomatous infiltration of aorta, carotid and coronary arteries
1935	Lane and Goodman [6]	7 F	Angina since 4 years of age; dyspnea	Rumbling systolic murmur at top of sternum; aortic snapping second sound; systolic thrill over carotid artery	B. P. 155/95; roentgenogram and electrocardiogram normal; father had xanthoma tuberosum
1939	Müller [4e]	31 F*	Angina for 10 years		
1942	Bloom, D.; Kaufman, S. R., and Stevens, R. A.: Arch. Dermat. & Syph. **45**: 1-18 1942	23 F	Sudden death	Blowing apical systolic murmur	Coronary sclerosis with myocardial degeneration
		18 M	Sudden death; poisoning (?); probably cardiac	Systolic murmur; increased aortic second sound	Siblings of previous patient
		14 F	Sudden death, typical of coronary disease; had one previous attack	.....	
		6½ F	Sudden death; cause (?)	.....	

* Patient was 21 years old when angina developed.

A review of the literature (table 2) revealed that in 20 cases of xanthoma tuberosum the patients were 31 years of age or less and had definite or probable associated heart disease. Eighteen patients were 21 years of age or less at the time of their first manifestations of cardiac disease. It has been recognized for more than fifty years than xanthoma tuberosum is often a familial disease.[2] It is not surprising, therefore, that in 11 of the 20 cases the patients had siblings with a similar condition—that is, with xanthomatosis and definite or apparent heart disease. In addition the father of 1 patient had xanthoma tuberosum.[3] Ten of the 20 patients (50 per cent) died suddenly, and another died as the result of cardiac failure at the age of 11. In the 3 cases in which necropsy was performed pronounced xanthomatous infiltration of the coronary arteries, aorta and large arteries was found, and in 1 infiltration of the mitral valves was noted. In 2 cases it was questionable whether or not rheumatic heart disease was present, and in 4 others cardiac murmurs were apparently the only manifestations of cardiac disease.

Coronary disease and angina pectoris are common among adults with xanthoma tuberosum,[4] but were present in only 3 of the reported cases in which patients were 21 years of age or less. In Fox's case,[5] reported in 1879, anginal symptoms occurred when the patient was 21 years old. The youngest patient who had xanthoma tuberosum with angina pectoris was reported by Lane and Goodman [6] in 1935. The patient was a girl 7 years of age who had had dyspnea and angina since the age of 4 years. Müller [4d] in 1939 reported the case of a woman 31 years of age who had had xanthoma tuberosum and angina pectoris since the age of 21.

NOTE.—When this article was in galley proof, we received from Dr. Conrad W. Giesen of Superior, Wis., the following added information: "This boy became my patient one week before he died. The day before his death I hospitalized

2. (*a*) Morichau-Beauchant, R., and Bessonnet, R.: Le xanthoma héréditaire et familial, ses relations avec la diathèse biliaire, Arch. gén. de méd. **192**:2313-2329, 1903. (*b*) Müller, C.: Xanthomata, Hypercholesterolemia, Angina Pectoris, Acta. med. Scandinav., 1938, supp. 89, pp. 75-84. (*c*) Török, L.: De la nature des xanthomes, avec quelques remarques critiques sur la notion des tumeurs; introduction, Ann. de dermat. et syph. **24**:1109-1156, 1893. (*d*) Wile, U. J., and Duemling, W. W.: Familial Xanthoma, Arch. Dermat. & Syph. **21**:642-647 (April) 1930.

3. Arning, E.: Ein Fall von familiärer Xanthomatose, abstracted, Arch. f. Dermat. u. Syph. **105**:290-291, 1910.

4 (*a*) Montgomery, H.: Xanthomatosis: A Systemic Disease, Proc. Staff Meet., Mayo Clin. **12**:641-644 (Oct. 13) 1937; (*b*) Cutaneous Manifestations of Systemic Disease, Minnesota Med. **22**:451-456 (July) 1939; (*c*) Cutaneous Manifestations of Diseases of Lipoid Metabolism, M. Clin. North America **24**:1249-1926 (July) 1940. (*d*) Müller, C.: Angina pectoris ved xanthomatose en arvelig sygdom, Nord. med. **2**:1183-1191 (April) 1939; (*e*) Angina Pectoris in Hereditary Xanthomatosis, Arch. Int. Med. **64**:675-700 (Oct.) 1939; (*f*) footnote *2 b*.

5. Fox, T. C.: A Case of Xanthelasma Multiplex, Lancet **2**:688-689 (Nov. 8) 1879.

6. Lane, C. G., and Goodman, J.: Xanthoma Tuberosum: Report of Familial Occurrence with Probable Cardiac Lesions, Arch. Dermat. & Syph. **32**:377-384 (Sept.) 1935.

him because of marked substernal pain and dyspnea on slightest exertion, and oxygen and aminophylline (theophylline ethylenediamine) were administered but with little or no effect on his pain and dyspnea. The following morning, Sept. 17, 1946 [one year after he had been examined at the Mayo Clinic] while propped up in bed eating his breakfast, he died very suddenly."

Dr. Giesen enclosed the observations at necropsy, furnished by Dr. G. L. Berdez of Duluth, Minn. The pertinent details from Dr. Berdez' report are as follows:

GROSS OBSERVATIONS

General Appearance.—Below the skin were several almost spherical tumors, measuring up to 5 cm. in diameter. The skin over many of the tumors was movable. The skin lining some of the tumors was fixed and a yellowish color could be seen through the thickness of the skin. The tumors were found below the skin of the elbows, of both hands, of the right knee, of both feet, of the left gluteal region and of the pinna of the right ear. Several fingers of both hands and several toes of both feet were considerably deformed by the tumors.

Tumors.—On cut surface, the tumors were rather compact, fibrous, pale yellowish and cloudy and were surrounded by a thin, fibrous capsule; they were difficult to shell out.

Heart.—The heart weighed 310 Gm. The cavities of the heart were dilated, mainly on the left side, and contained much partly clotted blood; there were small hemorrhages of the epicardium. The cusps of the aortic valve were thickened and fibrous, and there was evidence of slight insufficiency of the valve. In the mitral valve were arteriosclerotic changes, grade 1. The tricuspid and pulmonary valves showed nothing of note.

Coronary Arteries.—In the coronary arteries were arteriosclerotic changes, grade 3, with extensive, cloudy, yellowish deposits and slight calcification in places. The lumens of the coronary arteries were narrow in places, mainly the lumen of the anterior descending branch. The orifices of the coronary arteries were extremely narrowed.

Anatomic Diagnosis.—This was recorded as follows: xanthoma tuberosum multiplex; coronary sclerosis, grade 3, with pronounced narrowing of the anterior descending branch and beginning anemic infarct of the left ventricle (lower half of the anterior wall); cusps of the aortic valve thickened and fibrous; hypertrophy and dilatation of the heart; congestion and edema of the lungs, grade 1; arteriosclerosis of the aorta, grade 3; serous cyst of the right kidney; fatty deposits of the papillae of the kidneys; central passive congestion, grade 1, of the liver and bilateral hydrothorax, mainly on the right.

MICROSCOPIC OBSERVATIONS

Heart.—The fibers of the myocardium were somewhat hypertrophic. The wall of the anterior descending branch of the left coronary artery was much thickened and the lumen was extremely narrow; the intima was much thickened and was the site of large deposits of material which stained red with sudan stain (lipids). Many of the fibers of the myocardium were loaded with fine droplets of fatty material; those fibers which showed fatty change were arranged in small groups. There were also places where the muscle fibers of the heart were atrophic and sometimes stained poorly; moreover, the interstitial connective tissue was slightly increased.

Lungs.—In the examined portions, the pulmonary tissue gavé evidence of diffuse congestion.

Kidneys.—The renal tissue was moderately and diffusely congested; some of the tubules contained a small amount of coagulated albuminous material. In the papillae of the kidneys there were several deposits of lime salts and of crystals of cholesterol; in those portions the interstitial connective tissue was moderately infiltrated, mainly with lymphocytes. In the interstitial connective tissue of the tips of the papillae of the kidneys were numerous groups of "foam cells" loaded with lipids.

Aorta.—The intima was the site of enormous thickening formed by fibrous tissue and calcification in several areas. The media and the intima were infiltrated with occasional lymphocytes.

Tumors.—The tumors of the skin and of the subcutaneous tissue were formed by a fibrous connective tissue in which were embedded numerous groups of rather large polyhedral or rounded cells with clear finely vacuolated cytoplasm. The tumor tissue was infiltrated with a few scattered lymphocytes. In preparations stained with sudan, the finely vacuolated larger cells (foam cells) were loaded with numerous droplets of material which stained red with sudan (lipids).

SUMMARY

A typical case of primary hypercholesteremic xanthomatosis with xanthoma tuberosum of the skin and tendons, aortic stenosis and angina pectoris is reported. The patient was a boy 13 years old. Significant electrocardiographic changes indicative of disease of the coronary arteries were found. A review of the literature revealed 20 cases of xanthoma tuberosum with definite or probable cardiac involvement among patients 23 years of age or less at the time the cardiac lesion developed. In 3 of these cases angina pectoris was present. It is believed that the cardiac lesions in the case reported herein were due to xanthomatous infiltration of the aortic valve and coronary arteries. This hypothesis is substantiated by necropsy in similar cases. Certainly the prognosis in all such cases must be guarded, since in 50 per cent of similar cases reported in the literature the patients died suddenly, obviously of cardiac disease.

PYLORIC STENOSIS IN TWINS

Review of the Literature and Report of a Case

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OCCURRENCE OF PYLORIC STENOSIS IN MONOVULAR AND BINOVULAR TWINS

MOORE,[1] in 1924, reported hypertrophic pyloric stenosis affecting each of monovular twins. He found no previous reports of the occurrence of this disease in 1 or both twins. This condition has subsequently been recorded in 53 sets of twins which are listed in table 1. Sheldon[2] first noted "that when pyloric stenosis affects uniovular twins, both infants show the condition," and "when pyloric stenosis affects binovular twins, the disease is likely to occur only in 1 twin." Three exceptions to this rule have been reported previously. As shown in table 2, the twins reported on by Lasch[3] are an exception to the first part of this rule, and Sheldon[2] reported the only other recorded instance in which only 1 of monovular twins had pyloric stenosis while the other twin was not affected and showed no signs of asymptomatic pyloric hypertrophy such as found in Lewis' case.[4] The third exception was recorded by O'Donnell and Klein,[5] who reported a case in which the disease affected both of binovular twins. A similar exception is reported in the following report of a case.

Raymond and Richard S., male twins, were born on Jan. 13, 1946, six days before the date on which they were estimated to be due. The pregnancy, the mother's first, had been normal. Labor was prolonged because the pains were weak and intermittent. Both presentations were cephalic. Raymond, the first born, presented a left occipitoposterior position and was easily delivered by forceps rotation. Richard was then delivered by podalic version and extraction.

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1. Moore, H. L.: Twins with Hypertrophic Pyloric Stenosis, South. M. J. **17**:187 (March) 1924.

2. Sheldon, W.: Hypertrophic Pyloric Stenosis in One of Uniovular Twins, Lancet **1**:1048 (May 7) 1938.

3. Lasch, W.: Konstitutionopathologie der "angeborenen Pylorasstenose," München. med. Wchnschr. **72**:1155 (July 10) 1925.

4. Lewis, F. L. K.: Pyloric Stenosis in Identical Twins, Brit. M. J. **1**:221 (Feb. 12) 1944.

5. O'Donnell, F. T., and Klein, J. M.: Pyloric Stenosis in Non-Identical Twins, Am. J. Dis. Child. **62**:1025 (Nov.) 1941.

TABLE 1.—*Reported Cases of Pyloric Stenosis in Twins*

Author	Year Reported	Type of Twinning	Comment
Redlin, G.: Deutsche med. Wchnschr. **49**: 415, 1923	1923	?	Boys: both affected; 1 died and 1 recovered
Moore [1]	1924	Monovular	Boys: diagnosis confirmed in each by operation; both recovered
Sauer [13a]	1924	?	Boys: diagnosis verified at necropsy
Davis, H. H.: J. A. M. A. **83**: 686, 1924	1924	?	Boys: diagnosis confirmed in each by operation; both recovered
Lasch [3]	1925	Monovular	Girls: the only 1 affected died of influenza before operation could be performed; necropsy report: "hypertrophy of pyloric region"
Monrad [7]	1927	?	3 sets in a total of 228 cases; sex unknown; 1 member of each set affected; all patients treated medically
Bilderback [6]	1928	Monovular	Boys: diagnosis confirmed in each by operation; 1 recovered; 1 died
Cockayne, E. A., and Sheldon, W. P. H.: Proc. Roy. Soc. Med. **21**: 1260, 1928	1928	Monovular	Boys: diagnosis confirmed in each by operation; 1 recovered; 1 died
Sommer, R.: Deutsche Ztschr. f. Chir. **232**: 398, 1931	1931	Monovular	Girls: diagnosis confirmed in each by operation; both recovered
Varden, A. E.: J. Pediat. **3**: 493, 1933	1933	Monovular	Boys: diagnosis confirmed in each by operation; both recovered
Redgate, J. W.: Brit. M. J. **2**: 725, 1935	1935	Monovular	Boys: diagnosis confirmed in each by operation; 1 recovered; 1 died 16 days after the operation of "acute thymitis"
deLange [11]	1936	Monovular	Boys: diagnosis confirmed by operation in each; both recovered; maternal aunt had pyloric stenosis
Halbertsma, cited by Brendle [13c]	?	Binovular	Sex unknown: 1 twin affected
Brendle [13c]	1937	Monovular	2 sets: 1 set boys and 1 set girls; all 4 children affected *
		?	1 set: sex unknown; both affected
Sheldon [2]	1938	Monovular	Boys: diagnosis confirmed in 1 by operation; he recovered; the other showed no signs of symptoms of the disease
		?	10 sets: 1 member each set affected; diagnosis confirmed in each by operation
		Binovular	12 sets: 1 member each set affected; diagnosis confirmed in each by operation
Card [15a]	1939	Monovular	Boys: diagnosis confirmed in each by operation; 1 recovered, 1 died
Ford, Brown and McCreary [17]	1941	Monovular	Boys, 2 sets: diagnosis confirmed in each (Davis, H. H.: J. A. M. A. **83**: 686, 1924); all recovered
		Binovular	9 sets: 1 in each set affected; diagnosis confirmed in each case by operation; all recovered: 2 girls, 7 boys
		?	Boys: only 1 affected; diagnosis confirmed by operation; recovered; the other twin died of unstated cause; was thought, thirteen years later, to have been identical
O'Donnell and Klein [5]	1941	Binovular	Boys: diagnosis confirmed in both by operation; both recovered
Lewis [4]	1944	Monovular	Boys: diagnosis confirmed in 1 by operation; recovered; other had no symptoms but had visible peristalsis, a palpable tumor, and roentgenogram when 3 months old showed "definite delay at the pylorus" of barium meal
Laubscher and Smith	1946	Binovular	Boys: diagnosis confirmed in each by operation; both recovered

* These cases were reported from the literature but no reference was given. They may be a duplication of those in the table and therefore were not used in the subsequent tables.

There were two placentas and two separate layers of membranes with each placenta, evidence of their being binovular twins. At birth Raymond weighed 5 pounds 15½ ounces (2,704.4 Gm.) and Richard weighed 5 pounds 3½ ounces (2,367.2 Gm.). Both children were breast fed, and on the fourth day each was given supplementary feedings of Similac. They progressed normally, and when discharged from the hospital on the thirteenth day after birth Raymond weighed 6 pounds 9½ ounces (2,990.9 Gm.) and Richard weighed 5 pounds 7 ounces (2,566.4 Gm.).

Their progress was uneventful until Feb. 5, 1946, when Richard vomited for one day. On February 11, he began to have projectile vomiting. The next day he was admitted to the hospital for observation. The vomiting increased in spite of sedation with phenobarbital and the administration of atropine. Lactic acid skim milk formula was given at this time. Gastric peristalsis was visible, but no tumor could be felt. A diagnosis of hypertrophic pyloric stenosis was made. On February 14 Raymond was admitted with similar symptoms of one day's duration. There was a palpable tumor in the right upper quadrant in addition to visible gastric peristalsis and projectile vomiting. Roentgenograms of each twin showed their stomachs greatly distended with gas and little gas in the intestines. No barium was given, as it was not considered necessary in order to establish the

TABLE 2.—*Occurrence of Pyloric Stenosis in Monovular and Binovular Twins*

Type of Twinning	Number of Sets of Twins Affected	Number of Sets in Which Both Twins Affected	Percentage in Which Both Twins Affected	Number in Which Only One Twin Affected	Percentage in Which Only One Twin Affected
Monovular	13	11	84.6	2	15.4
Binovular	24	2	8.4	22	91.7

diagnosis. The treatment was the same as that given Richard. In addition both twins were given fluids subcutaneously to correct their dehydration.

On February 16 both twins were operated on, and a typical hypertrophied pylorus was found in each. A Rammstedt type of operation was performed on each child through a muscle-splitting incision in the right upper quadrant. Local anesthesia was used in each child. They improved rapidly after operation and are now robust and healthy. Raymond weighed 14 pounds 6 ounces (6,520 Gm.) and Richard 13 pounds 13½ ounces (6,279 Gm.) when 3½ months of age.

There is no history of pyloric stenosis in the family of either parent. The paternal grandmother had twin brothers. The blood type of both twins is type O, that of the mother is type A and that of the father type O. The mother is Rh negative and the father is Rh positive. The twins are both Rh negative.

COMMENT

In hypertrophic pyloric stenosis there is little doubt that the hypertrophy of the pyloric muscle is present at birth. Obstruction is occasionally present early in life, as in Keyser's case,[6] in which there was vomiting fourteen hours after birth and the diagnosis was confirmed by operation when the patient was 5 days old. One of us (J.H.L.) has

6. Bilderback, J. B.: Hypertrophic Pyloric Stenosis Occurring in Premature Twins, Northwest Med. **27**:182 (April) 1928.

seen a similar proved case in a 7 day old infant, and Monrad [7] recorded 30 cases in which symptoms appeared before the babies were 1 week old. The hypertrophic pylorus may not always cause symptoms.[8] Ladd and Gross [9] on the basis of observations at autopsy attribute the obstruction to edema following the trauma of food passing through a narrowed hypertrophic pylorus.

A review of the literature of pyloric stenosis in twins reveals some interesting evidence modifying some of the theories of its cause. There are many who have expressed the opinion that a genetic factor contributes to the disease and have cited instances of its occurrence in siblings, in successive generations and in other patients of varying kinship. Bilderback [6] reported two families in each of which 2 consecutive male children had pyloric stenosis. Schreiber [10] recorded an infant operated on for pyloric stenosis whose father and paternal grandfather had had pyloric obstruction, which, in each case, was thought to be due to a congenital anomaly (probably hypertrophic pyloric stenosis) although they did not have symptoms until adult life. Monrad's evidence that the hypertrophied muscle becomes normal as the child grows older casts some doubt on the diagnosis of these adults' condition. Hypertrophic pyloric stenosis in the maternal aunt of twins with the disease was reported by deLange [11] who also recorded another family in which 5 siblings were so affected and cited other instances of pyloric stenosis in relatives. Fabricius and Vogt-Møller [12] diagnosed the condition in all 4 of one mother's children. The first child had a different father from the other 3. Concurrent infection in 2 of these children, 1 of whom had bile-stained vomitus, raises a question as to the cause of the vomiting. All 4 were treated medically, and in none was a tumor palpable. Autopsy on 1 who died of pneumonia when 5 months old revealed "hypertrophy of the pyloric part of the stomach." Other instances of multiple cases in one or more generations of a family are reported.[13]

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7. Monrad, S.: Kurze Mitteilung über 228 Fälle von Stenosis pylori congenita, Monatschr. f. Kinderh. **37**:473, 1927.

8. (*a*) Lewis.[4] (*b*) Findlay, L.: Hypertrophic Pyloric Stenosis Without Symptoms, Arch. Dis. Childhood **12**:399, 1937.

9. Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood, Philadelphia, W. B. Saunders Company, 1941, p. 1.

10. Schreiber, G.: Familial Hypertrophic Pyloric Stenosis of the Nursling and Delayed Hypertrophic Pyloric Stenosis, Acta pædiat. **16**:562, 1933.

11. deLange, C.: A Contribution to the Pathology of Identical Twins, Arch. Dis. Childhood **11**:39 (Feb.) 1936.

12. Fabricius, B., and Vogt-Møller, P.: Contributions to the Problem of Heredity of Congenital Pyloric Stenosis, Hospitalstid. **80**:166 (Feb. 9) 1937.

13. (*a*) Sauer, L. W.: Hypertropic Pyloric Stenosis, Arch. Pediat. **41**:145 (March) 1924. (*b*) Monrad.[7] (*c*) Brendle, E.: Familiäres Vorkommen von

(Footnote continued on next page)

The diagnosis is in doubt in some of these cases and, as they are all isolated instances, no definite conclusions concerning any genetic factor can be determined. No evidence is available to show that the occurrence in relatives is more frequent than could happen by chance.

Lasch [3] pointed out that the occurrence of pyloric stenosis in one of monovular twins is evidence against a genetic factor although he suggested that further study of the occurrence in twins is necessary before a definite opinion can be formed. In favor of the genetic theory, however, is the fact that when 1 of monovular twins is affected the other is also nearly always affected. Of the two recorded exceptions to this rule, there is some question as to whether Lasch's [3] patient had pyloric stenosis.[2] It is possible that in the other case, Sheldon's,[2] the unaffected twin had hypertrophy of the pylorus without symptoms, as in Lewis' case and as Findlay has reported in single births.[15]

Because 80 to 85 of the patients with pyloric stenosis are males, Stolte [16] postulated that the hormones which are responsible for the hypertrophy of the musculature in pregnancy are transmitted through the placenta or the milk of the mother to the child and cause a hypertrophy of the musculature of the uterus in female infants and of the pylorus in males. This theory is not tenable in cases in which only 1 of binovular male twins is affected and when the female of binovular twins is affected and the male is not.

Ford, Brown and McCreary [17] suggested that "the environmental handicap imposed before birth on members of multiple sets is one factor inducing the condition of pyloric stenosis." They base this on the assumption that pyloric stenosis is about twice as frequent in twins as in single births. It will be shown that the reported cases do not confirm this assumption.

Pylorospasmus, Monatschr. f. Kinderh. **68**:295, 1937. (*d*) O'Donnell and Klein.[5] (*e*) Fabricius and Vogt-Møller.[12] (*f*) Cockayne, E. A.; Moncrieff, A. A., and Sheldon, W. P. H.: Familial Cases of Hypertrophic Pyloric Stenosis, Proc. Roy. Soc. Med. **21**:1261, 1928. (*g*) Cockayne, E. A.: Congenital Pyloric Stenosis in First Cousins, Lancet **1**:898 (April 28) 1934. (*h*) Finkelstein, H.: Säuglingskrankheiten, Amsterdam, Elsevier, 1938. (*i*) Caulfield, E. J.: Familial Incidence of Pyloric Stenosis, Am. J. Dis. Child. **32**:706 (Nov.) 1926. (*j*) Collins, J. D., in discussion on Rhodes, R. L.: Imperforate Anus, Ann. Surg. **123**:877 (May) 1946.

14. Footnote deleted on proof.

15. (*a*) Card, T. A.: Hypertrophic Pyloric Stenosis in Twins, J. Pediat. **14**:658 (May) 1939. (*b*) Lewis.[4]

16. Stolte, cited by deLange.[11]

17. Ford, N.; Brown, A., and McCreary, J. F.: Evidence of Monozygosity and Disturbance of Growth in Twins with Pyloric Stenosis, Am. J. Dis. Child. **61**:41 (Jan.) 1941.

INCIDENCE OF PYLORIC STENOSIS IN TWINS

Sheldon [2] reviewed 1,000 cases of pyloric stenosis in which treatment was given at The Hospital for Sick Children, Great Ormond Street, London, between 1912 and 1936. In this series there were 23 sets of twins. In the only set known to be monovular both twins were affected, and in each of the remaining 22 sets only 1 twin had the disease. In these the ratio of twins to infants born singly is 1 : 42.48 (1 in 43.48 cases). There were a total of 24 twins affected in the 23 sets. When this figure is used the proportions are 1 twin affected in 41.66 cases, or a ratio of 1 : 40.66. According to Sheldon's figures of "1 twin birth for every 80 single births," there would be 2 twin babies in every 82 babies born, or 1 twin in 41 children. This is a ratio of 1 twin to 40 children born singly. Note that this is practically the same ratio as that of twins having pyloric stenosis to single infants with the condition (1 : 40.66). Ford and her colleagues [17] reported 12 sets of twins in a series of 436 children treated for pyloric stenosis at The Hospital for Sick Children, Toronto, Canada. In this series the ratio of twins to infants born singly is 1 : 35.3, or 1 in 36.3 cases. Fourteen of the 24 twins had pyloric stenosis, a ratio of 1 : 30.1, or 1 twin in 31.1 infants affected. In this series the proportion of twins affected is a little greater than their proportion of the total births. Monrad [7] reported the only other series of cases in which the incidence of twins is recorded. In his series 1 twin was affected in each of three sets of 228 cases of pyloric stenosis, a ratio of 1 : 75, or 1 twin in 76 cases. This ratio is about half as great as the ratio of twins to infants born singly.

When these three series are combined in a total of 1,664 cases of pyloric stenosis, there are 41 twins affected in 38 sets, a ratio of 1 : 39.6 or 1 twin in 40.6 cases (table 3).

If it is assumed that the incidence of twin births is "1 in 83.4 births," [17] there would be 1 twin to 41.2 infants born singly or 1 twin in 42.2 children. As this is about the same ratio as for pyloric stenosis in twins to pyloric stenosis in infants born singly (1 : 39.6 or 1 in 40.6) it would seem that a twin is no more likely to be affected than is an infant who is not a twin. This does not support the assumption of an environmental handicap.

PROPORTION OF MONOVULAR AND BINOVULAR TWINS AFFECTED BY PYLORIC STENOSIS

Twenty-five per cent of twin births are monovular, a ratio of 1 : 3.[18] It would be interesting to know whether pyloric stenosis is more likely to affect one type of twin than the other. There are only two series of

18. McQuarrie, I. H.: in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company., Inc., 1946, vol. 1, chap. 3, p. 15.

cases in which this information is included (table 4). In Sheldon's [2] series of 23 sets of twins, 1 set was monovular, 12 sets were binovular and in 10 sets the type of twinning was not known. Of those in which the type of twinning was known only 7.7 per cent were monovular. In the series reported by Ford and her colleagues,[17] there were 2 sets of

TABLE 3.—*Incidence of Pyloric Stenosis in Twins*

	Total Cases of Pyloric Stenosis Reported	Sets of Twins in Which One or Both Twins Were Affected	Number of Cases of Pyloric Stenosis in Twins	Ratio of Twins Affected to Infants Born Singly Affected	
				Sets	Twin Children
Sheldon [2]	1,000	38	41	1:42.5 (1 in 43.5)	1:40.7 (1 in 41.7)
Ford, et al.[17]	436	12	14	1:35.3 (1 in 36.3)	1:30.1 (1 in 30.1)
Monrad [7]	228	3	3	1:75 (1 in 76)	1:75 (1 in 76)
Total*	1,664	38	41	1:42.8 (1 in 43.8)	1:39.6 (1 in 40.6)

* Bilderback [6] reported both members of 1 set of twins affected in "over 60 cases." As the total number in his series was not definitely stated they are not included in the above tabulation. When they are included and only 60 cases counted the ratios become 1:43.2 (1 in 44.2) and 1:39.1 (1 in 40.1).

monovular and 9 sets of binovular twins and 1 set in which the type of twinning was unknown. Of the 11 sets, 18.2 per cent were monovular. When the two series are combined, 12.5 per cent of those in which the type of twinning is known were monovular. If one includes all the

TABLE 4.—*Proportion of Monovular and Binovular Twins Affected with Pyloric Stenosis*

	Monovular Sets	Binovular Sets	Ratio of Monovular to Binovular Sets	Percentage of Monovular Sets
Sheldon [2]	1	12	1:12	7.7
Ford, et al.[17]	2	9	1:4.5	18.2
Total	3	21	1:7	12.5
All others in which type of twinning is known	10	3	3.3:1	77.0
Total*	13	24	1:1.84	35.1

* If, in the 17 cases in which the type of twinning is not known, one assumes that those in which both twins were affected are monovular and those in which only 1 twin was affected were binovular, the figures are 16 monovular to 38 binovular, or 29.6 per cent monovular twins. This is not a significant variation from the percentage of monovular twins in twin births.

cases reported in which the type of twinning is known, 35.5 per cent are monovular. This high percentage may be explained by the fact that cases are more likely to be reported when both twins are affected than when only 1 twin is affected and, as has been shown, this nearly always occurs in monovular twins. More accurate information will be

available when more series of cases of pyloric stenosis are reported in which the type of twinning is recorded.

SUMMARY AND CONCLUSIONS

The reported cases of pyloric stenosis in twins have been reviewed. When a monovular twin is affected the other twin will probably also be affected. There have been two exceptions in 13 sets of monovular twins reported. If a binovular twin is affected the other twin will probably not be affected. There have been two exceptions in 23 sets of binovular twins reported. The second exception is reported in this paper. A twin has about the same chance of having pyloric stenosis as an infant born singly.

The usual occurrence of pyloric stenosis in both of monovular twins is evidence in favor of a genetic factor in the causation of pyloric stenosis. Isolated instances of occurrence in siblings in successive generations and in patients of varying kinship have been reported. This is also suggestive of a genetic factor, but until this problem has been studied in large series of cases it is impossible to determine whether the occurrence is more than a coincidence.

Further study of series of cases is also necessary to determine whether one type of twin is more likely to have pyloric stenosis than the other.

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

QUANTITATIVE INVESTIGATIONS ON THE FORMATION OF UROBILINOGEN FROM BILIRUBIN. W. J. H. BUNGENBERG DE JONG, Nederl. tijdschr. v. geneesk. **86**:2405 (Sept. 26) 1942.

Indirect (anhepatic) bilirubin is not the sole source for the formation of urobilinogen. The author tries to prove this by clinical observations and by experiments in vitro.

VAN CREVELD, Amsterdam, Netherlands.

Metabolism; Infant Feeding; Milk and Other Foods

AN UNUSUAL SOURCE OF ERROR IN BASAL METABOLISM DETERMINATION. LEON J. WARSHAW, New York State J. Med. **45**:83 (Jan. 1) 1945.

It is pointed out that incorrect determinations of the basal metabolic rate are sometimes made because of leakage of oxygen from the apparatus. This makes it appear that the patient has utilized a larger quantity of oxygen and results in an apparently higher metabolic rate.

A case history is presented in which the initial readings for the basal metabolic rate were plus 198 and plus 201. It was found that the patient had a 5 mm. perforation in his right ear drum. When this ear canal was plugged with cotton soaked in liquid petrolatum, the rate dropped 140 points. Repetition of the experiment gave the same results.

The case is presented as an example of an unusual source of error in this procedure.

DAVIS, Rochester, N. Y.

PHYSICOCHEMICAL REGULATION OF RESPIRATION AND ACID-BASE EQUILIBRIUM IN CHILDHOOD. H. BRÜHL, Ann. pædiat. **160**:17 (Jan.-Feb.) 1943.

All authors interpret the carbon dioxide-combining power and p_H of the blood in infantile rickets as symptoms of metabolic acidosis.

Whether in infantile tetany there is acidosis or alkalosis is still undecided. A survey of the literature reveals that nearly all data concerning the blood (carbon dioxide-combining power, actual carbon dioxide content and p_H) point in the same direction but that their interpretation differs widely for various reasons: 1. The methods partly lacked exactness and certainty. 2. There is no agreement regarding the standard figures for infancy and childhood. 3. Often clinical cases were chosen by the authors in an unsuitable way. 4. It has been overlooked that there are different stages of infantile tetany in its clinical and physicochemical respects. 5. There were difficulties and lack of clarity in physicochemical definitions.

The author's results and the results of previous investigations are to be interpreted in a uniform way under the following conditions: 1. A strict differentiation has to be made between arterial and venous blood. Furthermore, it has to be noted whether during the drawing of the blood there was any hyperpnea or stasis. 2. The blood drawn from the cerebral sinus is significant for the cerebral metabolism. The acid-base equilibrium of the body can be judged on the basis of arterial analyses only. 3. The physicochemical data for infantile tetany have to be classified according to the different clinical stages and have to be interpreted separately. 4. As all authors agree that infantile tetany originates in infantile rickets, all

physicochemical data observed in tetany have to be compared with those for rickets instead of with the normal data, as has always been done previously. 5. By using Van Slyke's diagram of acid-base regulation and by drawing the "dotted line" into it according to Peters and Van Slyke, one can differentiate between the characteristics of the blood in "primary gaseous alkalosis" and in "primary metabolic acidosis."

The normal figures for carbon dioxide-combining power, actual pressure of the carbon dioxide and the p_H are given by the author for the different ages of infancy and childhood. The low carbon dioxide-combining power and its low pressure in infancy are due to a central hyperpnea which is characteristic for the metabolism of infants. Both the pressure of carbon dioxide and its combining power are lowered to such an extent that the resulting p_H in infants is almost the same as in adults and remains constant during the whole life. There is a parallel rise of the pressure of carbon dioxide and its combining power during growth.

The following results have been obtained by statistical survey of the results of previous investigations and of those of the author: 1. In rickets there is a compensated or uncompensated acidosis of the blood. 2. In latent tetany there is a "primary carbon dioxide-deficit" (acapnia) in the blood. 3. In cases of tetany with laryngospasms and other spasms there is a "primary carbon dioxide deficit" as well as a "primary alkali deficit" (metabolic acidosis) at the same time. 4. In cases of tetany with eclamptic convulsions there is a compensated or uncompensated metabolic acidosis in the blood.

By physicochemical analyses of the different stages of selected cases of tetany the statistical observations have been confirmed. Furthermore, the following details were observed: The carbon dioxide dissociation curve of the blood of the same child in both the rachitic and the tetanic stage does not change its position in the diagram. But as a consequence of a hyperpnea combined with the onset of the tetanic symptoms, the pressure of carbon dioxide is lowered on the constant curve and the p_H is shifted in the alkaline direction. This shows that the metabolism of rickets is not altered when tetanic symptoms appear, but the rachitic acidosis is covered (superposed) by a "primary carbon dioxide deficit" and by an "anacidosis" of the p_H.

This hyperpnea is essential for the understanding of the acid-base equilibrium in rickets and tetany. It originates in the increased irritability of the respiratory center parallel to the sudden changes in the ion quotient (Loeb); the p_H is seen to shift back and forth. In other words, acidosis and anacidosis alternate as often as hyperpnea gives way to normal breathing, and vice versa.

When spasmophilia is progressing through the state of laryngospasms to general convulsions, the peripheral acidosis due to muscular metabolism comes into the foreground more and more: the primary deficit in carbon dioxide glides over into a real metabolic acidosis.

AUTHOR'S SUMMARY.

Vitamins; Avitaminoses

RICKETS: A STUDY OF CALCIUM AND PHOSPHORUS METABOLISM. JESSE R. GERSTLEY, DAVID J. COHN and GRACE LAWRENCE, J. Pediat. **27**:521 (Dec.) 1945.

The writers question whether the type of carbohydrate used in an infant's formula influences the retention of calcium and phosphorus. Bergeim has shown that calcium and phosphorus are absorbed best when the intestinal contents are acid, and Gerstley has demonstrated that lactose added to diluted cow's milk leads to a stool more acid than does maltose-dextrin. Can the widespread usage of maltose-dextrin be responsible for the present day tendency to increasing dosages of vitamin D?

The metabolic and clinical observations extend over a period of ten years and are limited to infants not over 6 months of age. No vitamin D was given

during the six month period, as the writers wished to determine the effect of food per se.

Babies receiving breast milk during the summer season show a uniform retention of both calcium and phosphorus, one day being almost identical to the next. In the winter the retentions are not so orderly, but in quantity are quite satisfactory.

Babies receiving boiled undiluted cow's milk in winter show disorderly retentions and frequent losses. Summer changes the picture to disorderly hyperretentions as compared to the breast fed; presumably the baby becomes hypermineralized.

Babies receiving dilutions of boiled cow's milk with additions of either lactose or Dextri-Maltose show surprisingly satisfactory retentions even in winter. Lactose seems to give slightly better results, but the differences are not striking.

Clinically, the babies on breast milk average the best, with those on milk dilutions with carbohydrate addition a close second. Of the latter, those on lactose had slight superiority. The babies on undiluted cow's milk were a poor third during the winter but improved rapidly during the summer season. Two babies on undiluted cow's milk with 12 per cent carbohydrate gained extremely rapidly and developed definite clinical rickets.

The writers reopen the subject of the weight curve. In their experiments they note that the more the baby's weight curve seems to parallel that of the breast fed, the less likely is that baby to develop calcium and phosphorus deficiencies and clinical rickets. The exception is the baby receiving undiluted cow's milk during the summer and gaining less rapidly than the breast fed. But the curve shows that the baby, though normal clinically, retains excessive amounts of the two minerals.

The writers believe that these studies point to the importance of diluting cow's milk in infant feeding and the dangers of the present tendency toward overfeeding, either in concentration or in quality of food.

The writers incidentally note that in mild clinical rickets the rosary appears long before any changes are found roentgenologically or in the chemical composition of the blood. They also suspect that repeated or chronic mild infections may be accessory causal factors.

AUTHORS' ABSTRACT.

A CASE OF RICKETS. S. FARILL and E. GÓMEZ JÁUREGUI, Bol. méd. d'hosp. inf., México **1**:75 (March) 1944.

M. L. S., a 3 year old girl, had had deformities of the lower limbs and wrists since the age of 14 months.

On examination in the hospital, the patient was found to have a bilateral genu valgum of about 130 degrees, a rachitic rosary, nodular enlargements on the ends and sides of the long bones and other special signs.

Both the roentgenograms and the laboratory furnished data to support the diagnosis.

The patient was treated with massive doses of vitamin D once a month, calcium glycerophosphate, balanced diet and corrective osteotomies.

MADERO, México, D.F., Mexico.

VITAMIN P. J. GROEN, Maandschr. v. kindergeneesk. **10**:337 (May) 1941.

It is probable that in lemon juice besides vitamin C some other substances are present which are necessary for nutrition. Whether the citrin discovered by Szent Györgyi is one of these substances is still questionable. The experiments with animals should be repeated with identified material. Several investigators used substances which surely are not identical with Szent Györgyi's citrin. In hemorrhagic diseases of the vascular type citrin acts satisfactorily. To obtain a

good test for the absence of vitamin P from the diet it is necessary to develop a better method for the determination of this vitamin.

VAN CREVELD, Amsterdam, Netherlands.

SOME CASES OF DYSVITAMINOSIS. A. F. A. S. van Westrienen, Maandschr. v. kindergeneesk. **11**:304 (July) 1942.

The author reported on 4 cases of dysvitaminosis in children.

In the first case a boy 12 years old had pseudohypophyseal cachexia, probably caused by a long-continued shortage of vitamin C in the food. Clinical symptoms of scurvy were lacking.

In the second case a girl 2 years old showed, together with gingival swelling (but no hemorrhages), edematous swelling of the subcutaneous tissue and slight skeletal changes such as occur when there is a latent deficiency of vitamin C. Also in this case, though typical symptoms of scurvy were lacking, the clinical symptoms disappeared with administration of extra fruit juice and ascorbic acid.

In the third case a baby of 8 months, taken to the hospital for mild post-morbillous encephalitis, showed clinical symptoms of scurvy, which developed twelve days after its entrance into the hospital. Probably the fact that the baby had been given twice pasteurized milk played a role here.

In the fourth case a baby of 16 months with laryngospasm got a milk-free diet, supplemented with breast milk. In the hospital the color of the skin gradually became yellow and finally orange, although there was no icterus. The carotin content of the serum was high and the vitamin A content low, both facts being probably due to the scarcity of fat in the diet and to the many infections from which the child had suffered. Clinical symptoms of a shortage of vitamin A were lacking, but the orange-yellow color of the skin was regarded as the alarming symptom of a deficiency of vitamin A.

VAN CREVELD, Amsterdam, Netherlands.

TOCOPHEROL (VITAMIN E) IN THE BLOOD SERUM. J. COUPERUS, Nederl. tijdschr. v. geneesk. **87**:541 (March 20) 1943.

The tocopherol content of the blood serum in men varies between 30 and 130 micrograms per 10 cc. of serum, while the values which generally occur are between 50 and 90 micrograms. This amount is practically constant during a day, a week or a month. If the administration of vitamin E is necessary during an illness, a dose thrice a day of 30 mg. of tocopherol acetate (Ephynal) orally is recommended. In this way the highest available content of tocopherol in the blood serum can be reached (140 to 200 micrograms per 10 cc.). Tocopherol is not present in urine or in cerebrospinal fluid.

VAN CREVELD, Amsterdam, Netherlands.

VITAMIN B COMPLEX AND THE SYNTHESIS OF BLOOD PROTEINS. C. A. GRAAFLAND, Nederl. tijdschr. v. geneesk. **87**:679 (April 10) 1943.

The various factors of the vitamin B complex are to be found in varying concentrations in sources of vegetable and animal origin. The author defends the hypothesis that these vitamin B factors of animal origin are also of importance for the building up of the proteins in the blood. This is in accordance with the fact that many vitamin B factors are growth factors. Also it may be possible that the proteins and erythrocytes in the blood are made in an analogous way. In 5 cases of edema caused by lack of nourishment, a distinct improvement in the albumin content was obtained by oral administration of dried beer yeast or by injections of vitamin B complex. Hyperproteinemia arising when the nourishment contains a sufficient quantity of animal proteins but is deficient in calories can be explained by the great production of proteins in the body, because most of these proteins are used to compensate for the lack of calories.

VAN CREVELD, Amsterdam, Netherlands.

Hygiene; Growth and Nutrition; Public Health

TABLES FOR PREDICTING ADULT HEIGHT FROM SKELETAL AGE AND PRESENT HEIGHT. NANCY BAYLEY, J. Pediat. **28**:49 (Jan.) 1946.

Recent studies carried out at the University of California on the relation of growth to skeletal age indicate that it is possible to estimate, within certain limits of error, the probable adult height of children whose growth is still incomplete.

Individual differences in velocities of maturing result in widely varying degrees of maturity among any random sample of children of the same age, especially during adolescence. But velocities of maturing are not related simply to growth in size. Children who mature early are large for their age, but small in relation to their degree of skeletal development, while the opposite is true of slow maturers. Furthermore, the sexes differ in their patterns of early and late maturing. Before 13 years early maturing girls are large and late maturing girls are small, while the reverse is true after this age. Late maturing boys are usually slender and long legged, small before puberty but eventually growing tall.

The tables presented in this study are based on data from two sources, 200 Massachusetts children observed in the Harvard Growth Study and 200 California children studied at the Institute of Child Welfare of the University of California. In both studies the same children were measured and examined roentgenologically at regular intervals for periods ranging from five to twelve years, and covering the chronologic ages of 6 to 18 or 19 years.

To secure a measure of relative growth, each child's height at any given time was expressed as a percentage of his own adult stature as measured after closure of the epiphyses of the bones in his hand, wrist and knee. When this was done, the percentage of mature height attained was found to be closely related to skeletal age as determined by the Todd standards. This relationship to skeletal age was found to be much closer than to chronologic age. It was found also that, after the age of about 9 years, the prediction of adult height is much more accurate if a child's skeletal age is taken into account in making the estimate. This is especially true during early adolescence when differences in physical maturity contribute so largely to differences in children's heights.

The system of predictions here described is based on measurements of normal children. The authors do not expect it to be applicable to cases of extreme deviation in which the regulators of growth are not functioning normally.

The tables have been constructed to facilitate the process of computing predicted height. In order to predict a child's mature height it is necessary to have an assessment of his chronologic age, his skeletal age (based on roentgenograms which have been compared with standards such as those of Todd or Flory), and his height, measured at the time that roentgenograms were taken.

It is hoped that the tables will have clinical usefulness in predicting the adult height of children whose growth is incomplete. Such knowledge has been sought by surgeons in estimating the effect of growth in certain forms of osteotomy, and more generally in the prediction and possible control, through endocrine therapy, of the growth of children who are exceptionally tall or short for their age.

AUTHOR'S ABSTRACT.

CHILDBIRTH ASSISTANCE IN EL SALVADOR. MARCO TULIO MAGAÑA and MIGUEL ANGEL GALLARDO, Bol. Inst. internac. am. de protec. a la infancia **19**:572 (Dec.) 1945.

The authors make the following recommendations: (1) that an attempt be made to get maternity insurance established in El Salvador; (2) that more facilities for assistance in childbirth be provided in hospitals throughout the country, the number of maternity beds in private and official hospitals be increased, and the

hospitals be given adequate technical staff and equipment for any operation required in the care of pregnant women; that facilities be provided for transportation to these hospitals from all parts of the country; (3) that the number of physicians be increased, and that they be distributed as evenly as possible throughout the country; (4) that the midwife be controlled through official records and adequate regulations, and (5) that the people be taught how to take the maximum advantage from the services at their disposal.

AUTHORS' SUMMARY.

DIETETIC SERVICES IN CHILDREN'S HOSPITALS OF SANTIAGO, CHILE. VICTOR ESCARDÓ Y ANAYA, Bol. inst. internac. am. de protec. a la infancia **19**:604 (Dec.) 1945.

The new organization of the dietetic services of the Hospital Calvo Mackenna, in Santiago, Chile, is described by the author, who recently visited the hospital.

In this new plan dietetic kitchens are established near the children's wards and receive the foods partially prepared from the main kitchen and from the milk station.

Children's food passes through three phases, the "rule," which is the result of technical action on the materials and of preparation in the main kitchens; the "allowance," which is the amount allotted each child in the dietetic kitchen, and finally the "portion," which is the quantity received by each patient.

The author comments on the position of the milk stations in relation to the main kitchens. In the new organization there is a tendency to unite milk stations with main kitchens, which seems now of questionable usefulness.

AUTHOR'S SUMMARY.

Prematurity and Congenital Deformities

THE ETIOLOGY AND PATHOGENESIS OF ARACHNODACTYLY. KAROLY GREINER and TIBOR VARGA, Ann. pædiat. **164**:259 (May) 1945.

The causation and pathogenesis of the arachnodactyly were investigated on the basis of 2 cases of mother and daughter. In neither of the 2 cases could the disease be explained on the basis of known causes (weakness, "exhaustion," etc.). Morphologic, functional and laboratory examinations were carried out; the results ruled out an endocrine disturbance. The mother was the first in her family to have the disease (first sporadic case in an adult). In the case of the daughter the various symptoms of the disease as well as the accompanying anatomic anomaly showed in exactly the same form and degree as in the mother—dominant inheritance. The search for abortive cases—"formes frustes"—was without success. Bauer's view regarding sporadic cases could be verified for the first time practically: The sporadically appearing alteration was dominantly inherited. The cause of the arachnodactyly is not to be found in the germ layers. The disease results through the uniting of pathologic genes which are the results of mutations. The arachnodactyly is accordingly to be considered an inherited disease and as certainly belonging to that group of diseases which result through the union of constitutional abnormalities and developmental anomalies.

AUTHORS' ABSTRACT.

A CASE OF MORQUIO'S DISEASE. L. J. VERHOESTRAETE, Maandschr. v. kindergeneesk. **11**:455 (Sept.) 1941.

The author reports a case of Morquio's disease (eccentro-osteochondrodysplasia) in a girl aged nearly 5 years, with clinical and roentgenologic symptoms. During the first two years of life the diagnosis was difficult to make. The difference between Morquio's and Hurler's disease (lipochondrodystrophy) is stressed.

VAN CREVELD, Amsterdam, Netherlands.

PROGERIA AND PROGEROID. E. GORTER, Maandschr. v. kindergeneesk. **12**:53 (Dec.) 1942.

Observation of a boy 9 years old who demonstrated a number of characteristics of progeria without having the disease in its typical form has induced the author to make a critical study of the recent literature on progeria and related diseases. He arrives at the following conclusions:

Progeria is a disease entity which can be conceived of as a combination of precocious senility and pituitary insufficiency, which principally affects the growth factor. Many symptoms could be explained by this pituitary insufficiency, but the symptoms of precocious senility remain as an independent group of unknown origin. The most characteristic symptoms of this group are the atheromatous changes of heart and vessels. The differences and the similarities of progeria and definite pituitary dwarfism are most pronounced in the description of cases in which there have been necropsies. Atypical cases of both conditions occur. These atypical cases show such a great resemblance among one another and differ so greatly from typical progeria that they can best be placed in a separate group under the name "progeroid." Besides his own case the author mentions 4 such cases from the literature.

VAN CREVELD, Amsterdam, Netherlands.

Newborn

CARDIOSPASM IN THE NEWBORN. PORTER P. VINSON, J. Pediat. **27**:565 (Dec.) 1945.

This is a report of a case of cardiospasm in the newborn. According to the author the "case is reported . . . to suggest that so-called cardiospasm in infancy is the result of temporary incoordination of the nerve-muscle mechanism of swallowing."

AUTHOR'S ABSTRACT.

THE GREENBERG MODIFICATION OF THE FLAGG LARYNGOSCOPE: ITS USE IN ASPHYXIA NEONATORUM. LESTER J. GREENBERG, J. Pediat. **27**:602 (Dec.) 1945.

The article presents the Greenberg Modification of the Flagg Laryngoscope further to facilitate its use in cases of asphyxia neonatorum.

The following is a summary of the advantages of the new type of laryngoscope with description of its use: 1. It affords easier approach to the larynx—the speculum is passed in midline and slid down the tongue to the epiglottis. 2. The tongue is immobilized without effort—the tongue comes to rest in the longitudinal trough of the lingual surface of the speculum, which is concave rather than convex. 3. There is relatively atraumatic immobilization and elevation of the epiglottis, exposing the rima without undue tension and consequent distortion of the rima—the epiglottis is lifted up out of the field of vision by the tip of the concave lingual surface on the terminal end of which the tubercle of the epiglottis comes to rest. The relative ease of this procedure diminishes the likelihood of increasing edema as a result of the procedure itself. It also decreases the danger of cardiac complications resulting from stimulation of the vagus nerve when forceful traction upward and forward is exerted on the epiglottis. 4. The ease of the passage of this instrument and ready localization of structures make repeated passage of the speculum unnecessary. 5. The field of vision is increased because of the retraction of the adjacent tissues by the slight upward tilt of the lateral angles of the speculum. 6. The features of the Flagg Laryngoscope which permit the passage of instruments for intervention from the right side as well as in midline are retained. 7. The common difficulty of the tongue's falling into the lumen of the laryngoscope and obstructing the view is avoided by the immobilization of the tongue.

Three cases of asphyxia neonatorum are presented to demonstrate the instrument in use—those of baby J. T., with obstruction of the rima glottis by clots of curdled

breast milk, of baby D. D., with cerebral injury and atelectasis and of baby F. C., with congenital stenosis of the larynx.

AUTHOR'S ABSTRACT.

INCIDENCE OF THE EIGHT RH TYPES AMONG 179 WHITE PUERTO RICANS. MERCEDES VICENTE TORREGROSA, Proc. Soc. Exper. Biol. & Med. **60**:215 (Nov.) 1945.

The Rh types among 179 white Puerto Ricans were determined and compared with the incidence of the types found in white persons and Negroes in New York city (Wiener, A. S.; Davidsohn, I., and Potter, E. L., *J. Exper. Med.* **81**:63, 1945). The Rh negative in the white Puerto Ricans was 10 per cent compared with 13 per cent and 8 per cent for white persons and Negroes respectively in New York. The following percentages were found in the various Rh types, percentages for white persons and Negroes of New York being given in parentheses: Rh_0, 15.08 (2.6, 41.2); Rh_1, 39.1 (54.1, 20.2); Rh_2, 19.54 (12.8, 22.4); $Rh_1\ Rh_2$, 13.97 (16.4, 5.4); Rh′, 1.68 (0.9, 2.7); Rh″, 0.55 (0.3, —). The author suggests that the differences in the incidence of Rh types may be explained on the basis of some unknown mixture with the Negro race.

HANSEN, Galveston, Tex.

THE RH FACTOR: RH SUBTYPE ISO-IMMUNIZATION IN AN "RH-POSITIVE" MOTHER. R. T. SIMMONS and G. A. KELSALL, M. J. Australia **1**:391 (April 21) 1945.

In a routine search for weak atypical agglutinins in certain maternity cases the authors discovered the presence of antibodies in an "Rh-positive" mother's serum which agglutinated her "Rh-positive" infant's cells and those of known "Rh-positive" controls. The infant appeared to be normal except for transient jaundice on the third day and a slight reduction in hemoglobin and red cell count observed on the twenty-first day. Further investigation indicated that the isoimmunization was due to a difference in Rh subtypes, the mother belonging to subtype Rh′ and the baby belonging to subtype Rh_1.

GONCE, Madison, Wis.

CONGESTION CAUSED BY COMPRESSION OF THE THORAX IN A NEWBORN CHILD. J. D. LEBRET, Maandschr. v. kindergeneesk. **10**:335 (May) 1941.

A newborn baby showed swelling and discoloration of and small hemorrhages in the face and upper part of the neck. These symptoms can be compared with the syndrome described by Perthes, Braun and Sick, and can be explained as the consequence of a compression of the thorax during parturition.

VAN CREVELD, Amsterdam, Netherlands.

Acute Contagious Diseases

EPIDEMIC MENINGITIS AND MENINGOCOCCEMIA TREATED WITH PENICILLIN. RALPH C. LOHREY and JOHN A. TOOMEY, J. Pediat. **28**:86 (Jan.) 1946.

Twenty-one patients with proved meningococcic infections were treated with penicillin. Fourteen of these patients had epidemic meningitis and were treated with penicillin intrathecally and intramuscularly. Eight patients responded satisfactorily; 6 did not respond so well to the doses administered. Four patients with epidemic meningitis were treated with penicillin intramuscularly only. Of these, 3 did not respond well to therapy, and 1 died. Four patients had meningococcemia and were treated with penicillin intramuscularly. Three recovered promptly. In 1 patient the infection progressed to epidemic meningitis.

The daily intrathecal and frequent intramuscular administration of penicillin is a tedious procedure. In the opinion of the authors, the results are not of sufficient value to warrant its use as a form of treatment in epidemic meningitis when simpler and more effective methods are available.

TOOMEY, Cleveland.

A Comparative Study of the "Immune Response" to Various Pertussis Antigens and the Disease. Leo Cravitz and John W. Williams, J. Pediat. **28**:172 (Feb.) 1945.

The primary objectives of this study were, first, to learn what factors are involved in immunity to pertussis and, second, to determine what constitutes an effective prophylactic agent against pertussis.

A series of animal experiments were conducted in a study of the antigenic quality of the Pertussis Antigen (Detoxified) (Lederle Laboratories, Inc.), Sauer's vaccine and Combined Pertussis Vaccine with Pertussis Endotoxoid (Ayerst, McKenna & Harrison, Inc.). In studying the "immune response" the authors utilized the following tests: agglutination, opsonocytophagic index, antitoxin titrations and intradermal reactions. In this direction they developed the agglutinin-opsonic index test which is a highly efficient test for the detection of both agglutinins and opsonins simultaneously. The results obtained indicate that (1) Sauer's vaccine gives rise to a substantial agglutination titer and opsonic index, as well as antibodies capable of neutralizing a dermonecrotic endobacterial antigen; (2) the detoxified antigen (Lederle Laboratories, Inc.) produces antitoxin in high titer and agglutinins in low titer, and (3) the combined bacterial vaccine and endotoxoid produces both antitoxin and bacterial antibodies in high titer.

Antibody titrations in human beings were performed at the Boston Health Department Well Baby Clinics, at the Roof Nurseries of the Health Units at the South Department of the Boston City Hospital and at the Morgan Memorial Day Nursery. Thus the authors were able to study the "immune response" in children who had been inoculated with Sauer's vaccine, the antigen of the Lederle Laboratories, Inc., and the combined vaccine with endotoxoid of Ayerst, McKenna & Harrison, Inc. They also studied the "immune response" during the course of illness and convalescence and in children who had had the disease in years past.

The results of their clinical studies of the "immune response" give the following indications: 1. In children immunized with Sauer's vaccine the production of bacterial antibodies is rapid, attaining maximum titer about two months after immunization. These antibodies may persist for several years but decrease more rapidly after the first year. 2. In children immunized with the antigen of Lederle Laboratories, Inc., the production of bacterial antibodies is minimal but the development of antitoxin in significant titer during the first two or three months is the predominating response. The decline of circulating antitoxin, however, was rapid and frequently was complete after six months. 3. In children immunized with the combined vaccine and endotoxoid the development of bacterial antibodies is similar to that in the children immunized with Sauer's vaccine but, in addition, there is also the production of antitoxin. 4. In a clinical infection with pertussis the agglutinins are formed earlier than the opsonins but the latter persist in higher titer after recovery. These antibodies can be demonstrated two to three years after recovery from the disease in a large percentage of cases. Little or no antitoxin can be demonstrated in the blood of persons who have recovered from the disease.

The Strean cutaneous test evokes an allergic response in children immunized with Sauer's vaccine, the antigen of Lederle Laboratories, Inc., or the combined vaccine of Ayerst, McKenna & Harrison, Inc.; a toxic inflammatory reaction in susceptible persons who have neither been immunized nor ill with pertussis, and a negative reaction six months after recovery from the disease. This test may conceivably be of value in determining susceptibility to pertussis providing a heated control is used.

The results of a field investigation indicate that the children immunized with Sauer vaccine were afforded substantial protection against pertussis for at least two years—the duration of the study. On the other hand, the Pertussis Antigen (Detoxified) of Lederle Laboratories, Inc., did not appear to offer any protection against an attack of pertussis but did modify the disease so that it was clinically milder in a majority of cases.

As a result of these studies the authors recommend the use of a combined phase I bacterial vaccine with pertussis toxoid for prophylaxis against the disease. The "immune response" to such a product more nearly corresponds to that produced by an attack of pertussis.

AUTHORS' ABSTRACT.

TREATMENT OF HEINE-MEDIN'S DISEASE WITH POTASSIUM CHLORATE. H. J. KOLK, Maandschr. v. kindergeneesk. **10**:323 (May) 1941.

The author gives criteria which may be used in determining the value of potassium chlorate in the treatment of patients with poliomyelitis. He discusses first, the character of the epidemic at Nymegen (Holland) in the autumn of 1939 (it consisted of 110 cases) and, second, the obvious tendency of patients with this disease to recover. This tendency can be concluded from the great number of patients with mild paresis who recovered spontaneously within a few days. His conclusions are somewhat in favor of the drug, though the number of cases was too small to justify a definite conclusion.

VAN CREVELD, Amsterdam, Netherlands.

A RARE CASE OF GANGRENE OF THE HYMEN AS A COMPLICATION OF MEASLES. A. C. ROSMAN, Maandschr. v. kindergeneesk. **10**:332 (May) 1941.

A rare case of gangrene of the hymen as a complication of measles in a 2 year old girl is reported.

VAN CREVELD, Amsterdam, Netherlands.

PSYCHOSES IN TETANUS AND DIPHTHERIA. P. A. H. BAAN, Nederl. tijdschr. v. geneesk. **87**:357 (Feb. 20) 1943.

First a psychosis following tetanus is described, but here, besides the tetanus bacillus, other noxae were present which could be considered the cause of the psychic disturbances. Then 2 cases of psychosis following diphtheria are described; in one of these the diphtheria could be shown to be the pathogenic factor. Hence, contrary to the general opinion in the psychiatric literature, a postdiphtheritic psychosis may occur.

VAN CREVELD, Amsterdam, Netherlands.

Acute Infectious Diseases

USE OF AMINO ACIDS IN A CASE OF SEVERE SALMONELLA SCHOTTMUELLERI (PARATYPHOID B) INFECTION IN AN INFANT. I. SEIDEMANN, J. Pediat. **28**:90 (Jan.) 1946.

The incidence of Salmonella infections in infants is not high. The literature on the subject is not abundant, especially with specific reference to the Salmonella schottmuelleri type of infection. The disease, when found, was usually not considered severe in infants, although various complications have been reported. A case of severe infection with S. schottmuelleri in an 18 month old child is presented. The dramatic response attributed to the parenteral administration of amino acids as added supportive therapy was considered of sufficient general interest to warrant presentation of the case.

The value of amino acids as additional supportive therapy in the treatment of children with S. schottmuelleri infections as well as other infectious diarrheas, appears to be deserving of consideration and should be studied further.

AUTHOR'S ABSTRACT.

THE USE OF GENTIAN VIOLET IN CHILDREN INFECTED WITH ASCARIS LUMBRICOIDES. H. W. BROWN, J. Pediat. **28**:160 (Feb.) 1946.

Wright and Brady (1940) suggest that the use of gentian violet medicinal for the treatment of patients with Enterobius (pinworm) infection is contraindicative

by the presence of Ascaris lumbricoides. This theoretic contraindication is based on the possibility that gentian violet medicinal might stimulate A. lumbricoides to migrate. The immersion of living A. lumbricoides in solution of gentian violet medicinal failed to demonstrate an irritative property of the drug. Twenty children infected with A. lumbricoides were given the routine ten day treatment with gentian violet medicinal as for pinworm. There was no evidence of stimulation of A. lumbricoides by this drug in terms of migration of the worms or the production of intestinal or pharyngeal obstruction. The A. lumbricoides egg count dropped 37 per cent after the gentian violet therapy.

AUTHOR'S ABSTRACT.

CONTRIBUTIONS TO THE TREATMENT OF OXYURIASIS AND LAMBLIASIS IN CHILDHOOD. J. C. PONCE, Rev. Soc. de pediat. d. Litoral **10**:102 (May-Aug.) 1945.

Eighty-nine cases of oxyuriasis and 29 of lambliasis were studied clinically. The biology and life cycle of the parasites are discussed, and the symptoms and treatment are described. In oxyuriasis, two ways of reinfection are possible: In the exogenous, eggs are transmitted from the anus to the mouth by the fingers, and in the endogenous, the eggs develop in the submucosa of the intestine. The role of oxyuriasis as the cause of appendicitis is stressed, living Oxyuris worms frequently having been found in the submucosa of diseased appendixes. The usual treatment with gentian violet medicinal was successful in 68 per cent; the failures were probably due to the lodging of the parasites in the submucosa. The Giardia lamblia may be a simple saprophyte, or it may cause a picture similar to amebic dysentery. The site of predilection is the small intestine, especially the duodenum. The parasite may also be found in the gallbladder. The symptoms are relapsing diarrhea of all degrees, from slight dyspepsia to severe mucosanguinolent stools. In all cases of relapsing diarrhea with abdominal pains lambliasis should be suspected. Nineteen patients were treated with quinacrine hydrochloride, 10 with Acranil (3-chloro-7-methyloxy-9-[2-hydroxy-3-diethylamino]-propylaminoacridine dihydrochloride), another acridine derivative. The treatment was successful in all cases.

SOLMITZ, Chicago.

THE PROBLEM OF VACCINATION AGAINST INFLUENZA. J. VAN DEN HOVEN VAN GENDEREN, Maandschr. v. kindergeneesk. **10**:462 (Sept.) 1941.

A review is made of the experiments performed at different laboratories to immunize test animals and also men against the virus of epidemic influenza. Immunization of ferrets, mice and swine has been proved to be possible; for human beings this possibility is still doubtful.

VAN CREVELD, Amsterdam, Netherlands.

PSEUDOTETANUS. J. H. SMIDT VAN GELDER, Maandschr. v. kindergeneesk. **11**:51 (Nov.) 1941.

The author gives a description of a case of pseudotetanus in a boy 9 years old. He tries to prove that the disease is not tetanus, or tetany, but is probably a toxicosis caused by Ascaris lumbricoides.

VAN CREVELD, Amsterdam, Netherlands.

ON A CASE OF LAMBLIASIS IN WHICH THE CLINICAL PICTURE WAS OF CELIAC DISEASE. L. M. C. BEDAUX, Maandschr. v. kindergeneesk. **12**:256 (June) 1943.

The author discusses the pathogenesis and clinical symptoms of lambliasis. He then reports a case in which a girl of 5 years had a number of symptoms typical of celiac disease; the sediment of the duodenal fluid was crowded with Giardia lamblia organisms. By treatment with Acranil (3-chloro-7-methyloxy-9-[2-hydroxy-3-diethylamino]-propylaminoacridine dihydrochloride) the general condition as well as the stools was quickly improved. The author gives as his opinion that the

lambliasis in this case probably had been aggravated by an epidemic hepatitis by which in turn a celiac syndrome was caused in the neuropathic patient.

VAN CREVELD, Amsterdam, Netherlands.

A NEW CENTER OF THE EPIZOOTIC AMONG FIELD MICE (THIRD COMMUNICATION). W. A. P. SCHÜFFNER and H. BOHLANDER, Nederl. tijdschr. v. geneesk. **86**: 2413 (Sept. 26) 1942.

From examination of field mice in the neighborhood of Warga (Frisia, the Netherlands) a great number of voles proved to be infected with Leptospira grippotyphosa. Therefore in the Netherlands there are a much larger number of infected mice than originally was assumed. It is remarkable that among human beings scarcely a case of the illness occurs, this in contradiction to what is found in other countries. One should remember that the clinical picture easily can be misunderstood.

VAN CREVELD, Amsterdam, Netherlands.

GENERALIZED MYCOTORULOSIS. A. C. ROSMAN, Nederl. tijdschr. v. geneesk. **86**: 2460 (Oct. 3) 1942.

A case of sprue in a girl of 2½ years is reported. At the age of 4 months sprue developed in the mouth. At the age of 1 year the skin was progressively involved. The mucous membranes of larynx and vulva were also affected. The unfavorable prognosis of generalized sprue is pointed out. Treatment with sulfapyridine and sulfamethylthiazole had had no favorable result when the child left the hospital.

VAN CREVELD, Amsterdam, Netherlands.

MUD FEVER IN FRIESLAND. P. MUNTENDAM, W. A. P. SCHÜFFNER and H. ZYSLING, Nederl. tijdschr. v. geneesk. **87**:397 (Feb. 27) 1943.

In central Friesland, where a serious epizootic of infection with Leptospira grippotyphosa was found among the field mice, 9 cases of mud fever were diagnosed. The patients all were agricultural laborers who were occupied with making hay and mowing.

VAN CREVELD, Amsterdam, Netherlands.

Chronic Infectious Diseases

TOXOPLASMOSIS IN A LARGE MINNESOTA FAMILY. FORREST H. ADAMS, RICHARD HORNS and CARL ECKLUND, J. Pediat. **28**:165 (Feb.) 1946.

A typical case of toxoplasmosis occurring in a 14 year old white girl is reported by F. H. Adams, R. Horns and C. Ecklund of the University of Minnesota Medical School and the Minnesota State Board of Health. The patient was the sixth of twelve children born to two normal adults of German extraction. Her complaints of headache and scotomas began at 12 years of age, but she was known to have had loss of central vision as early as 9 years of age. Shortly before her admission to the hospital, headaches and vomiting became the prominent symptoms. Physical examination revealed a bilateral chorioretinitis and papilledema of the eyes with considerable loss of visual acuity in the right eye. There was a slight reduction of hearing in the right ear, and there were a hyperactivity of the knee and ankle jerks bilaterally. The results of routine blood tests were normal. Roentgenograms of the skull revealed increased intracranial pressure and one area of calcification. Ventriculograms showed an internal hydrocephalus. Neutralization tests with the patient's serum showed the presence of Toxoplasma organisms.

Treatment of the patient consisted of coagulation of the choroid plexus of the right lateral ventricle. This was done to offset the disturbed secretion-absorption

balance of the cerebrospinal fluid probably caused by the Toxoplasma organisms. After this procedure the patient had immediate cessation of symptoms except for occasional scotomas. Psychometric testing revealed an intelligence quotient of 109, in spite of the hydrocephalus which was known to exist.

The rest of the family was investigated. Neutralization tests elicited positive reactions for Toxoplasma in the mother and in 9 of 10 siblings tested. One sibling died at birth, and hence could not be tested, but it was known to have had an enlarged head possibly due to toxoplasmosis acquired in utero. The mother and 10 siblings had no clinical symptoms or signs of toxoplasmosis as determined by physical or roentgenologic examination. The authors point out that toxoplasmosis is probably commoner than previously suspected and that it should be considered in the differential diagnosis in all cases showing hydrocephalus, microcephaly, chorioretinitis, cerebral calcification, convulsions, encephalitis and atypical pneumonia accompanied by a spotted fever–like rash.

AUTHORS' ABSTRACT.

DISPLACEMENT OF THE MEDIASTINUM DUE TO PULSION BY A CASEOUS TUBERCULOUS LUNG WITHOUT PLEURAL EFFUSION. JOHN FLEEK MILLER and B. H. KEAN, J. Pediat. **28**:200 (Feb.) 1946.

In a review of texts and available periodical literature, the authors found no mention of mediastinal shift due to pulsion by a caseous lung without the presence of pleural effusion.

An 8 month old boy entered the hospital with "noisy breathing," cough, diarrhea, vomiting and loss of weight. He was malnourished and acutely and chronically ill and breathed with difficulty. There was ballooning of the intercostal spaces on the left and the left side of the chest was more expanded than the right. The apex beat of the heart was observed and felt in the costal angle. Percussion of the heart borders was unsatisfactory, but the heart beat was flat to percussion and breath sounds were absent over the entire left lung. The right side of the chest was normally resonant, and there were no rales or abnormality of breath sounds. A roentgenogram of the chest was reported to show massive pleural effusion on the left displacing the heart and mediastinum to the right.

A thoracentesis of the left hemithorax was done on the day of admission, and a small amount of white caseous material was obtained on negative pressure. This contained a myriad of acid-fast bacilli on smear.

The patient had a downhill course and died one week after admission.

On autopsy, the pertinent findings were limited to the thorax. When the thorax was opened it was observed that the trachea, the heart and the mediastinum were shifted to the right. The left pleural cavity was obliterated by dense fibrous adhesions between the visceral and parietal surfaces. No free fluid was present. The left lung was greatly enlarged. This enlargement had distended the left hemithorax and had caused a displacement of the mediastinum to the right. Sectioning of the left lung revealed that virtually the entire parenchyma was one solid mass of white or yellowish white, nonaerated, caseous material. No cavities were present. Microscopic examination showed extensive caseation necrosis. Only here and there were a few pulmonic alveoli recognized. There were some small patches of caseation necrosis in the right lung.

The chief interest in the case lies in the similarity of the clinical and roentgenologic observations with those of pleurisy with effusion. However, after caseous material had been obtained on thoracentesis, the correct diagnosis might have been suspected.

AUTHORS' ABSTRACT.

A STUDY OF HYPERERGIC REACTIONS. G. POPOVICIU, Ann. pædiat. **160**:84 (Jan.-Feb.) 1943.

The author's observations, the first results of which were published in 1936 to 1938, confirm the existence of the hyperergic, proximally stronger cutaneous

reaction in fresh, active or activated tuberculous processes, observed for years by Mayerhofer and his co-worker Skrivanel and described in the literature from 1939 to 1941. Popoviciu's publications were made independently of Mayerhofer, whose work (originally published in the Serbo-Croatian literature before 1939) became available to him only in 1941. The author concurs with Mayerhofer's analysis and opinion and confirms the hyperergic character of these unequal reactions with his still incomplete experiments concerning (1) the comparative study of the other tuberculin reactions (Moro, Moro-Scarzella-Popoviciu, Trambusti, Mantoux) with the proximally stronger Pirquet reaction; (2) the level of the blood calcium and phosphorus (generally elevated in fresh, active tuberculosis with unequal Pirquet reaction), and (3) the clinical (including roentgenologic) study of his cases of the previous fifteen years. The practical, the diagnostic, the prognostic and the therapeutic value of the asymmetric hyperergic Pirquet reaction increase especially in wartime, when the active or activated tuberculous processes are more frequent not only in children, but also in adults.

AUTHOR'S SUMMARY.

TUBERCLE OF THE CAUDA EQUINA. J. DROOGLEEVER FORTUYN, J. DRUKKER and H. M. VAN DER LINDE, Maandschr. v. kindergeneesk. **11**:227 (May) 1942.

A boy 2 years old with tuberculosis of the lungs gradually showed a caudal syndrome. This syndrome was caused by a solitary tubercle of the cauda equina.

VAN CREVELD, Amsterdam, Netherlands.

MILIARY TUBERCULOSIS IN THE GUISE OF PURULENT MENINGITIS. A. C. ROSMAN, Maandschr. v. kindergeneesk. **12**:41 (Oct.-Nov.) 1942.

A case of tuberculosis miliaris and meningitis tuberculosa in a girl 11 years old is described. After typhoid, lasting about three weeks, meningitis developed. The septic state of the blood, the purulent serum and the negative Pirquet reaction made the diagnosis purulent meningitis the most probable. The necropsy, however, showed extensive tuberculosis miliaris with purulent exudation at the base of the brain.

VAN CREVELD, Amsterdam, Netherlands.

THE INFLUENCE OF BOVINE TUBERCULOSIS ON TUBERCULIN TESTS OF SCHOOL CHILDREN. D. DE VRIES and L. WERKHOVEN, Nederl. tijdschr. v. geneesk. **88**:472 (May 20-27) 1944.

In an investigation of the reactions to tuberculin tests shown by school children in the northern part of the province "Noord-Holland" in the Netherlands the author obtained peculiar results. In two communities (on the island of Texel and in the formerly isolated community Wieringen) the percentage of children with positive reactions to tuberculin tests was strikingly smaller than in all other communities. The differences could not be explained by differences in income or condition of living and could be explained only partly by a difference in the mortality from tuberculosis, causing a larger possibility of infection of healthy children. It appeared, however, that the percentages of positively reacting animals (cattle) in the two communities with a low percentage of positively reacting children were much smaller than in the other communities. The isolation of Texel and the former isolation of Wieringen give a good explanation of the more favorable condition of the cattle in these two communities and also of the smaller number of positively reacting children. In the communities of Texel and Wieringen the examined children—ranging in age from 6 to 15 years—were during their whole life, as regards the possibility of infection with bovine tubercle bacilli, in much more favorable circumstances than were the children in the other communities.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Blood, Heart and Blood Vessels and Spleen

PAROXYSMAL TACHYCARDIA. EDWIN P. SCOTT and M. A. LIMPER, J. Pediat. **28**:96 (Jan.) 1946.

The authors report 2 cases of paroxysmal tachycardia in infancy. In one patient the paroxysmal tachycardia was relieved by intravenous administration of quinine dehydrochloride.

The paroxysmal tachycardia and congestive failure returned, and the child died while quinine dehydrochloride was being administered intravenously.

In the second case the paroxysmal tachycardia was discovered more or less accidentally. Treatment was successful with Digifolin administered intramuscularly.

AUTHORS' ABSTRACT.

ADHESIVE POSSIBILITY OF LEUKOCYTES: A TREATMENT OF THE PHYSIOLOGY OF LEUKOCYTES. F. BUSER, Ann. pædiat. **160**:299 (May-June) 1943.

It is shown that the adhesiveness of the white blood cells is a function of only the granulocytes (granulated cells of the myeloid system) and the monocytes, and is lacking in the lymphocytes. The index of adhesiveness (number of adherent cells per unit of surface per thousand granulocytes and monocytes per cubic millimeter of blood) is remarkably constant in different ages (except the neonatal period).

In the course of various acute infectious diseases as well as chronic infectious and noninfectious diseases the index of adhesiveness remains for the majority of the cases within the range of the normal controls. In severe toxic states, however, the index of adhesiveness may be considerably reduced. But there is no regular correlation between the prognosis and the degree of the adhesiveness. Also in toxic diseases with unfavorable outlook the index of adhesiveness may be within normal limits. On the other hand, some diseases with good prognosis (e. g. nephritis) may show a low index.

These observations disagree with those of the previous investigators, who calculated their results on the basis of equal adhesiveness of all white blood cells, including lymphocytes (which Buser states is erroneous).

It is shown that the adhesiveness of the leukocytes is linked with the process of coagulation of the blood.

AUTHOR'S SUMMARY.

THE INDEX OF FIXATION OF LEUKOCYTES IN HEALTHY INFANTS. C. RIVIER and G. ROSSIER, Ann. pædiat. **164**:101 (March) 1945.

In order to compare their results with those of other authors Rivier and Rossier have prepared two indexes, one for granulocytes and the other for leukocytes. The index of adhesiveness is lower in the infant than in the adult: the younger the child the lower the index. In the first ten days of life the index is especially low. Change in diet and fasting are without importance.

The index is not dependent on the number of leukocytes. Even in the case of considerable temporary leukocytosis the percentual relationship of the adherent leukocytes remains almost constant. It is remarkable that one can determine the constancy of the index of adhesiveness in view of the character of the method and the possibility of error.

AUTHORS' SUMMARY.

A CASE OF CARDIOMEGALIA GLYCOGENICA. J. H. P. JONXIS, Nederl. tijdschr. v. geneesk. **87**:308 (Feb. 13) 1943.

In a case of cardiomegalia glycogenica, in which the patient died at the age of 4 months, the glucose metabolism could be examined in pieces of living muscle tissue. The demolition of the glycogen appeared not to differ from that in normal

pieces of muscle. The cause of the accumulation of glycogen in this case probably may be explained by a shifting of the reaction glucose-1-phosphate ⇄ glycogen + phosphoric acid in the direction of the glycogen synthesis.

VAN CREVELD, Amsterdam, Netherlands.

SURGICAL TREATMENT OF THE PATENT DUCTUS ARTERIOSUS. H. O. WYNEN, Nederl. tijdschr. v. geneesk. **87**:697 (April 10) 1943.

A case of surgical treatment of patency of the ductus arteriosus is described. During the operation the blood pressure was under regular control. Both in this case and in one reported on by Praag (*Nederl. tijdschr. v. geneesk.* **86**:633 [March 14] 1942) the operation was sucessful.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Nose, Throat and Ear

RHINOLOGY IN CHILDREN: RÉSUMÉ OF AND COMMENTS ON THE LITERATURE FOR 1944. D. E. S. WISHART, Laryngoscope **55**:381 (Aug.) 1945.

The common cold is caused by a virus. Secondary invaders produce the complications. The peaks of incidence of colds are in September-October, January-February and April-May. The incubation period is twenty-four to thirty-six hours. The spread of colds could be controlled by isolation of the infected persons. Other methods of prevention have been disappointing. Vaccines and vitamins have not been of value. Intranasal spraying of vaccine, however, has at least a scientific basis. Sulfonamide compounds are effective as preventives, and codeine and papaverine seems to shorten the duration of the cold. Crowe believes that irradiation to eliminate excessive lymphoid tissue is of great value; he believes that this reduces the number of colds and infections of the upper respiratory tract.

Many methods of treatment are mentioned. Frequent local use of the sulfonamide drugs may be of value. Use of nonirritating shrinking solutions, spot suction, irrigation with isotonic solution of three chlorides (Ringer's solution) and not allowing the bedroom temperature to be below 50 F. are advocated by Schall as methods of treatment. Cold vaccines, whether given by mouth or by hypodermic injection, have not proved effective.

Treatment of sinusitis in children should be directed to the region of the middle turbinate, for it is in this region that many of the sinuses drain. Wishart condemns interference with the inferior turbinate, washing the maxillary sinus by the natural ostium and some other rather widely used procedures. He stresses personal after-care following sinal operations.

Tonsils should be removed only when so enlarged that they interfere with swallowing or when they are chronically infected. Adenoids should be removed when they obstruct the air passages, the sinuses or the eustachian tubes. The relationship of tonsillectomy to poliomyelitis is discussed. Birdsall enumerates and evaluates signs and symptoms commonly regarded as reasons for removing tonsils and adenoids. Many of these symptoms attributed to diseased tonsils and adenoids are really due to sinusitis. Penicillin therapy has great possibilities as a cure of osteomyelitis of the frontal bone and perhaps even of cavernous sinus thrombosis. Fox reports excellent results in the treatment of epistaxis by intramucosal injection of a sclerosing agent.

Eosinophilia in polyps and in nasal smears is an indication of allergy, although its absence does not rule out allergy.

Hilding has made observations on the manner of the natural drainage of the sinuses. The relationship of the lymphatics to diseased sinuses is discussed.

Graves and Edwards discuss in detail the function and the structure of the eustachian tubes. The pharmacology and the effects of various shrinking solutions on the nasal membranes have been studied by Lierle, Evers and others.

Pastilles of penicillin have apparently helped local infection of the mouth and throat.

There has been nothing new of note recently in the treatment of atrophic rhinitis.

Some surgical procedures are discussed. Eisenstodt believes that conservative submucous resection might often be used in children, with no interference with the subsequent development of the nose.

Nasal trauma is commented on. Imperatori describes a Mackenty operation on a child with atresia of the pharynx following tonsillectomy and adenoidectomy.

Several reports of tumors are mentioned.

HITSCHLER, Philadelphia. [ARCH. OTOLARYNG.]

ACUTE LARYNGOTRACHEOBRONCHITIS IN CHILDREN. T. HALBERTSMA, Maandschr. v. kindergeneesk. **11**:97 (Jan.) 1942.

Three cases of acute laryngotracheobronchitis in children were observed by the author; 1 of the children died. The morbid picture is discussed. Especially characteristic is a tough, viscous, mucoid secretion in the trachea and the bronchi, which can be removed only with great difficulty and which obstructs the large and small branches of the bronchi. The mortality is about 50 per cent. The therapy is discussed.

VAN CREVELD, Amsterdam, Netherlands.

TWO NEUROGENIC INTRATHORACIC TUMORS. G. M. H. VEENEKLAAS, Maandschr. v. kindergeneesk. **12**:211 (May) 1943.

The author describes 2 cases of intrathoracic neurogenic tumors. In both cases the shadow caused by the tumor on the roentgenogram had three characteristics: (1) The shadow rested with its greatest diameter against the vertebral column; (2) the shadow was situated in the posterior mediastinum, and (3) the shadow was opaque with homogenous density and with regular sharp borders.

In the first case the tumor was found in a boy aged 5 years, who had general complaints. When the patient was 7 years old the tumor was removed by operation. At the pathologic examination it proved to be a ganglioneuroma of the sympathetic nerve. Later a severe kyphoscoliosis developed.

In the second case the tumor was found in a girl aged 5 years with no complaints at all; the child was under medical control for more than twelve years during which time the tumor grew proportionally with the child.

The author reviews the intrathoracic forms of ganglioneuroma and neurinoma in the literature.

VAN CREVELD, Amsterdam, Netherlands.

THE TREATMENT WITH ANTISERUM OF ACUTE LARYNGITIS CAUSED BY HEMOPHILUS INFLUENZAE. ROBERT G. JORDAN JR. and J. RENDER TURNER, J. Pediat. **27**:572 (Dec.) 1945.

Four cases of acute laryngitis caused by Hemophilus influenzae are presented. The clinical picture of high temperature, shock, acute laryngitis, leukocytosis with predominance of polymorphonuclear cells, positive blood cultures and history of sudden onset was first described by Sinclair. Several cases have been reported, early tracheotomy and adequate sulfonamide therapy being recommended.

In 92 to 95 per cent of cases of influenzal meningitis the organisms have been type B. Alexander believes that the capacity of sulfonamide compounds to effect complete recovery from type B, H. influenzae infection is influenced by two factors: (*a*) The infection must be relatively mild and (*b*) the drug must be started early in the course of the infection. She believes that only under such conditions will

sufficient time be afforded for the patient to produce through his own powers sufficient antibody to overcome the disease.

The sudden onset and the need for emergency treatment are emphasized. Three of the 4 patients presented were treated with H. influenzae, type B rabbit antiserum. The one who was not treated with antiserum died, in spite of early tracheotomy and sulfadiazine and penicillin therapy in adequate amounts. One patient treated with antiserum was a sibling of the one who died.

The three patients treated with H. influenzae type B rabbit antiserum made rapid, uneventful recoveries.

It would seem that in these cases of influenzal laryngitis, the best results can be expected with the use of type B antiserum in addition to sulfonamide compounds and penicillin. Apparently the use of antiserum is life saving in some cases. When used early, it probably prevents the necessity of tracheotomy.

AUTHORS' ABSTRACT.

Diseases of Lungs, Pleura and Mediastinum

AGENESIS OF THE LUNG: A CASE REPORT. ARNOLD WIDERMAN and CLIFFORD H. PETERS, J. Pediat. **28**:204 (Feb.) 1946.

An 8 month old girl, brought in for treatment of an infection of the upper respiratory tract, was found to lack normal pulmonary sounds on the right, a sign associated with a shift of the mediastinum and heart to the right. The usual complaints of a cardiopulmonary disease were completely absent. Further, careful investigation of the birth, past history and development revealed nothing suspicious.

The results of roentgenologic and fluoroscopic examination of the chest agreed with the results of physical examination. There was a shift of the heart to the right side of the chest, lack of aeration of the right side of the chest and compensatory emphysema of the left lung. In addition, there were minor bony anomalies of the spine and the ribs. Air trapped in the tracheobronchial tree after attempted bronchoscopy permitted clear roentgenographic visualization of the trachea and the left bronchus. No right bronchus could be seen.

In a brief review, the following points were noted. The anomaly is rare and usually diagnosed only after death. In itself the condition is compatible with life. Because the anomaly is frequently associated with congenital anomalies of other vital organs and because there is greater susceptibility to pulmonary infections, the prognosis is in doubt. The lesion probably results from a failure of development in utero, and the degree ranges from hypoplasia to complete absence of the lung, the bronchus and the vascular supply on the affected side.

AUTHORS' ABSTRACT.

PULMONARY CYSTS IN EARLY INFANCY. H. WILLI, Ann. pædiat. **164**:113 (March) 1945.

Three cases are reported of pulmonary cysts, each different from the others, which were observed from the time of birth and for several months and even years.

In the first case a large congenital pulmonary cyst is dealt with. At first filled, it emptied in the first three months and then persisted in this condition in the following years.

In the second instance an infected cyst of the lung is dealt with. The infection resulted during birth from aspiration of infected amniotic fluid. The cyst disappeared in two and one-half months, probably as a result of the obstruction of the bronchus which drained it. The obstruction was the result of inflammation.

The third is that of a giant postpneumonic cyst. This cyst persisted many months and finally healed in a short time as a result of Monaldi's drainage.

A congenital cyst with mediastinal pneumatocele is also described.

AUTHOR'S SUMMARY.

LOBECTOMY IN THE TREATMENT OF BRONCHIECTASIS IN CHILDREN. H. WAMSTEKER, Maandschr. v. kindergeneesk. **12**:1 (Oct.-Nov.) 1942.

The author gives a review of the surgical therapy of bronchiectasis, especially of the one stage lobectomy, which he has tested experimentally, modified and refined. Three cases are described in detail. In his series of twenty-four lobectomies in children and adults there occurred no dangerous postoperative complications. In the one stage operation the recovery was quick, especially in children. The author pleads for surgical consultation, after a pediatric one, for children with bronchiectasis.

VAN CREVELD, Amsterdam, Netherlands.

TRANSITORY EOSINOPHILIC INFILTRATIONS OF THE LUNGS IN CHILDHOOD. J. M. BUWALDA, Maandschr. v. kindergeneesk. **12**:188 (April) 1943.

Three cases of eosinophilic infiltrations of the lungs in children are described. From these descriptions it is evident how difficult it is to differentiate the diagnosis of this and of tuberculous infiltrate and how divided opinions are about the treatment of patients with eosinophilic infiltration. Finally, the author describes a case in which there were all the characteristics of a transitory infiltration but eosinophilia was absent.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

THE SURGICAL TREATMENT OF THE MORE COMMON TYPES OF DIAPHRAGMATIC HERNIA. STUART W. HARRINGTON, Ann. Surg. **112**:546 (Oct.) 1945.

Although diaphragmatic hernia occurs less often than the other types, there are more varieties than occur through all the other walls which encase the abdominal contents. The author prefers to classify them into two main groups, nontraumatic and traumatic.

A nontraumatic diaphragmatic hernia may be congenital or acquired. If congenital it usually does not have a hernial sac. The commonest sites of a congenital hernia in the probable order of frequency are as follows: (1) through the hiatus pleuroperitonealis; (2) through the esophageal hiatus; (3) through an anterior substernal opening, and (4) through the gap left by partial absence of the diaphragm. If the hernia is acquired after birth, the sites of occurrence are as follows: (1) through the esophageal hiatus; (2) through the region of fusion of the anlage of the diaphragm, and (3) at sites named under the congenital type.

The author discusses in detail the surgical considerations and surgical treatment of the various types of diaphragmatic hernia.

BANTIN, Omaha.

TREATMENT OF ACUTE SUPPURATIVE PAROTITIS IN INFANTS. EDWARD E. D. NEUHAUSER and BENJAMIN G. FERRIS JR., J. Pediat. **27**:589 (Dec.) 1945.

For many years the accepted therapy for acute suppurative parotitis in adults has been small doses of roentgen radiation. This method has been thoroughly successful in curing the condition without the necessity of surgical drainage.

Acute suppurative parotitis in infants has been recently reported by Sanford and Shmigelsky, and the clinical entity adequately described. They found a total of 62 cases in the literature including their 5 cases. They felt that it was probably commoner than the literature indicated. Administration of sulfathiazole by mouth and surgical intervention was their treatment of choice.

In the past three years the authors have had 3 patients with acute suppurative parotitis in the newborn period, and 1 older patient, a girl, who had acute suppurative parotitis associated with generalized staphylococcic septicemia. All the patients in the newborn period had their disease one day prior to treatment, and they all responded promptly in two to six days. The older child responded similarly but eventually succumbed to the septicemia.

Treatment consisted in roentgen therapy to the involved areas on consecutive days for two to three days. All the patients in the newborn period received sulfadiazine, and 1 also received penicillin. The blood levels varied from 3.5 to 17.4 mg. per hundred cubic centimeters. The child with septicemia received sulfadiazine first and later sulfathiazole. This was before penicillin was available. From all 4 patients Staphylococcus aureus was obtained on culture of the pus expressed from the parotid duct.

In all 4 patients the parotid involvement disappeared in two to six days without recurrences. This period included the period of treatment. This was a much shorter period than that reported by Sanford, which varied from two to three weeks. Furthermore, this method of therapy avoided surgical intervention and the possibility of a deforming scar or parotid fistula.

Chemotherapy was given these patients as well as roentgen therapy to control any additional infection which might have been present. In the future penicillin probably can be used along with roentgen therapy, especially if Staphylococcus aureus is present. In cases of milder disease without added infection roentgen therapy alone should be sufficient.

This condition is considered an emergency, and roentgen therapy should be administered as soon as the diagnosis is established or suspected. It has been the authors' custom to administer 125 r to the involved parotid glands on the first day. They have used 125 kilovolts, 53 milliamperes, a 3 mm. aluminum filter, and a 15 inch 38.1 cm. target-skin distance with a half value layer of 4.6 mm. of aluminum. A similar dose is given on the second day. If there has been decided improvement, as is usually the case, no further treatment is given. If improvement is slight roentgen therapy should be repeated on the third day. The authors have not had to give more than three treatments, but in rare instances in which more radiation is deemed advisable a fourth treatment could be given on the fourth or fifth day. If there has been no improvement by the fourth treatment it is doubtful whether any more roentgen irradiation would be of value. In the unusual instance in which the patient does not respond to roentgen therapy surgical intervention might be warranted.

AUTHORS' ABSTRACT.

INFANTILE DIARRHOEA. PATRIA GAIRDNER, Arch. Dis. Childhood **20**:22 (March) 1945.

The author reports on a study of 216 cases of diarrhea in children under 15 months of age. These children were in three groups: 69 were in institutions, 25 had recently been discharged from institutions and 122 had no institutional history.

The death rate was 67 per cent among infants less than 1 month old, and in the entire number of cases 109, or 51 per cent, died. In forty-seven postmortem examinations otitis media was observed in 12 cases, mastoiditis in 4, bronchopneumonia in 8 and otitis and pneumonia in 10. The author points out that in this study there was a high incidence of parenteral infections but that treatment was most successful with nonabsorbed sulfasuxidine.

KELLY, Milwaukee.

ATRESIA OF THE ESOPHAGUS ASSOCIATED WITH OTHER MALFORMATIONS. CARLOS HERRERA ROMERO, Bol. méd. d. Hosp. inf., México **1**:37 (May-June) 1944.

N. A. L., a 2 day old girl, was admitted to the ward for premature infants with a weight of 2,360 Gm. and a temperature of 35 C. (95 F.). There was a constant and abundant mucopurulent secretion from the nose. There were also symptoms of bronchopneumonia. The routine treatment of the ward was initiated. Twelve hours later the first feeding was administered with a dropper, but it was regurgitated after only a few cubic centimeters had passed. Then a catheterization was done, but the catheter was stopped at a certain point, and the tip came out through the mouth. This fact, together with the roentgenologic studies, resulted in the diagnosis of atresia of the esophagus.

The department of pathology reported the finding of other malformations, of the circulatory system, pyloristenosis, etc.

MADERO, México, D. F., Mexico.

TWO CASES OF INTUSSUSCEPTION FROM MECKEL'S DIVERTICULUM IN WHICH CURE WAS EFFECTED. JESÚS LOZOYA S., Bol. méd. d. Hosp. inf., México **1**:64 (May-June) 1944.

J. L. M. A., a 5 month old boy, was admitted to the hospital two days after he had become ill. The chief complaints were general malaise, continuous crying, vomiting, fever and enterorrhagia. At the examination a mass was felt near the hepatic angle. The mass was also felt on digital examination, and there was mucus. The patient was successfully operated on, and a Meckel diverticulum was found included in a necrotic portion of the intestine. The postoperative course was stormy but was controlled with appropriate measures. The patient was discharged, completely cured, eleven days later.

The second case was also of a 5 month old boy who became suddenly ill. The diagnosis, observations, operation and the progress were similar to those in the first case. He was also discharged cured in eleven days.

MADERO, México, D. F., Mexico.

PRESENT STATUS OF TREATMENT OF ACUTE NUTRITIONAL DISORDERS IN EARLY CHILDHOOD. J. DEUTSCH, A. GOLDMANN and E. NASSAU, Ann. pædiat. **164**: 129 (March) 1945.

The use of sulfathiazole and sulfaguanidine has been recommended in the treatment of dyspepsia, intoxication, dysentery and enteritis in infants and small children. Successful results have been reported. The curative effect is ascribed to the increased permeability of the cells or their increased power of absorption with respect to sulfonamide compounds. This view is supported by experimental investigations. Tea should be given and, in some cases, liquids should be administered intravenously or intratibially. Food preparations such as dextrin-maltose should not be given. Milk, whole or 50 per cent diluted, with the usual sugar suffices. The mortality in 35 cases of gastroenteric intoxication was 11.5 per cent. However, there were complications in all the fatal cases, and the intoxication was secondary.

AUTHORS' SUMMARY.

CONGENITAL ATRESIA OF BILIARY DUCTS WITH LATE OCCURRING ICTERUS AND FECAL ACHOLIA. G. KLACKENBERG, Ann. pædiat. **164**:145 (March) 1945.

A case of malformation of the biliary passages is discussed here. A 7 week old child was admitted to the hospital with cerebral hemorrhage as a result of hypoprothrombinemia. One week before admission biliary stasis had been established.

The late appearance of jaundice and acholia does not exclude the possibility of congenital atresia of the biliary ducts.

AUTHOR'S SUMMARY.

NORMAL VALUE OF PANCREATIC FERMENT IN DUODENAL JUICE OF CHILDREN. A. DREYFUS, Ann. pædiat. **164**:337 (June) 1945.

A short description is given of the method usually practiced at the Children's Hospital of Basle to determine the lipase in the duodenal secretion.

The pancreas ferment values which have been found by other authors for the duodenal secretion are given.

AUTHOR'S ABSTRACT.

DUODENAL KATHEPSIN. E. FREUDENBERG, Ann. pædiat. **166**:77 (Feb.) 1946.

From the duodenal juice of children, by means of a Ryle tube, a protease was obtained the qualities of which differ considerably from pepsin, trypsin and erepsin. It resembles kathepsin, however, as found in the gastric juice.

By adequate treatment of the genuine duodenal juice with organic acids at 55 C. and at p_H 2.5 this protease could be separated from trypsin. This procedure destroys the erepsin as well. Peptones are not catabolized by the preparation. Alkaline reaction has a reversibly suppressing influence on the enzyme, but if exposure to alkaline reaction is prolonged the enzyme is irreversibly destroyed. Bile acids retard the effect of the enzyme also. In an acid milieu (p_H 2.5 to 3) the enzyme is stable and can be kept for many weeks in a refrigerator; it can be kept for shorter periods even at 37 C.

The thus purified juice was used to determine its activity on milk, gelatine, ovalbumin, edestin and gliadin. The optimum p_H varies, according to the protein used, from 3.7 to 4.5.

The protease can be activated by hydrogen sulfide and cystein. The greatest increase was shown when the enzyme was used on gelatine; no increase was noted when cows' milk was used.

The optimum temperature for the action of the enzyme was astonishingly high, 60 C., but the metabolism was even higher at 70 than at 40 C.

Formation of plastein under suitable conditions was a distinct property of this protease. Formation of plastein, caused by pepsin, is probably due to the content of kathepsin in the pepsin preparation.

Kathepsin could be demonstrated in the meconium of 2 premature babies, born in the fifth and sixth months of pregnancy, respectively, who died soon after birth.

Pavlov was the first to find a protease in the duodenal mucosa of dogs. The purpose of this article is to elucidate the chemical and physiologic nature of Pavlov's protease.

AUTHOR'S SUMMARY.

Nervous Diseases

LISTERELLA MENINGITIS. N. I. HANDELMAN, C. C. ROTONDO, E. P. SCOTT and H. T. KNIGHTON, J. Pediat. **28**:210 (Feb.) 1946.

A case of meningitis in a 6 week old infant caused by Listerella monocytogenes and treated with sulfadiazine and penicillin with recovery is reported.

The causative organism was found to be fifteen to twenty times as resistant to penicillin as is Staphylococcus aureus. Therefore, by exclusion, the authors concluded that sulfadiazine may be the therapeutic agent of choice in similar infections.

AUTHORS' ABSTRACT.

TUMORS IN THE SPINAL CANAL IN CHILDHOOD: II. ANALYSIS OF THE LITERATURE OF A SUBSEQUENT DECADE (1933-1943); REPORT OF A CASE OF MENINGITIS DUE TO AN INTRAMEDULLARY EPIDERMOID COMMUNICATION WITH A DERMAL SINUS. WALLACE B. HAMBY, J. Neuropath. & Exper. Neurol. **3**:397 (Oct.) 1944.

Hamby reports that in a survey of the literature in 1933 reports of 100 cases of intraspinal tumors in children of 15 years or younger were found. In the subsequent decade (1933-1942, inclusive) 114 such cases were reported. The distribution of neoplasms in the combined series was as follows: gliomas, 20.6 per cent; sarcomas, 19.6 per cent; dermoids, 17.3 per cent; neurinomas, 10.7 per cent; lipomas, 4.7 per cent; meningiomas, 4.7 per cent; chloromas, 4.2 per cent; tumors of blood vessels, 3.3 per cent; tumors of the sympathetic nervous system, 2.8 per cent, and miscellaneous tumors, 12.1 per cent. In all, there were 21 "hourglass tumors," a percentage of 9.8. Seven cases of spinal epidural cysts are described in the literature of the last decade.

Hamby reports the case of a 3½ year old boy who recovered from influenzal meningitis and a subsequent attack of meningitis. Several surgical procedures were performed. At first a sacral dermal mass was incised and drained. Finally, an

infected epidermoid cyst, extending from a sacral dermal sinus into the congenitally elongated spinal cord, was evacuated but could not be completely freed from the surrounding neural tissue.

GUTTMAN, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

A CASE OF MULTIPLE CYSTICERCOSIS OF THE ENCEPHALON WITH ARACHNOIDITIS OF THE FOURTH VENTRICLE IN A BOY SEVEN YEARS OLD. ROBLES, Bol. méd. d. Hosp. inf., México **1**:21 (March) 1944.

The subject of this article was admitted with the complaints of cerebral vomiting, frontal headache, right ophthalmodynia, vertigo, somnolence and tonic convulsive crisis. The illness had begun two years previously and the symptoms had made their appearance in the order stated.

The chief laboratory findings were: the presence of persistent eosinophilia, the Pandy and Nonne-Apelt reaction, + + +, in the spinal fluid and negative reactions to the Wassermann and Kline tests. The roentgenograms and encephalograms showed a separation of the sutures, digital impressions, a slight widening of the sella turcica and a bilateral and symmetric dilatation of the lateral and median ventricles.

Clinically, there was papilledema, presence of the Romberg sign and ataxic gait. There is a family history of teniasis.

With all these data, the diagnosis was made. A craniectomy was performed, and the progress was favorable for the first two weeks, but gradually the patient began to go downhill, and he died three weeks later.

The pathologist found 1,858 cysticerci distributed throughout the entire encephalon.

MADERO, México, D. F., México.

CALCIFIED TUMOR OF THE RIGHT PARIETAL LOBE (PROBABLY A TUBERCULOMA). FERNANDO LÓPEZ CLARES, Bol. méd. d. Hosp. inf., México **1**:32 (May-June) 1944.

P. B. O. was admitted to the hospital after having convulsions and other symptoms typical of epilepsy. There also was a history of pulmonary tuberculosis in the grandmother. The child is microcephalic.

By roentgenologic examination a calcified mass was found in the right parietal lobe which was thought to be a tuberculoma, although the reaction to the Mantoux test was negative and the evidence in the roentgenogram of the chest was dubious.

The patient was successfully operated on a few days later, and went home cured.

The department of pathology reported that the specimen was made up of calcified necrotic tissue in which, with some difficulty, some elements could be distinguished which indicated the previous existence of tissue of specific chronic infiltration of tuberculous type.

MADERO, México, D. F., Mexico.

PNEUMOCOCCIC MENINGOENCEPHALITIS CURED WITH SULFAPYRIDINE. F. LÓPEZ CLARES, Bol. méd. d. Hosp. inf., México **1**:49 (March) 1944.

The author reports on 2 cases of pneumococcic meningoencephalitis in which a cure was effected with sulfapyridine. In the first case an 18 month old girl suffered a trauma of the head the day before admission to the hospital. Both ears were discharging pus. The clinical impression was that of meningoencephalitis with otitis media purulenta, but pneumococci were demonstrated in the spinal fluid. The child received 1 Gm. of the drug for a period of fifteen days. The second patient was a boy 16 months of age, for whom the same diagnosis was made. He received sulfapyridine, 0.20 Gm. per kilogram of body weight for seven days and 0.10 Gm. per kilogram for six days more. He also received vitamins, etc. Both patients recovered, but the first one was left as a sequel a right hemiplegia.

MADERO, México, D. F., Mexico.

A Case of Pneumococcic Meningitis in an Infant. E. Travella and R. Pineda, Rev. Soc. de pediat. d. Litoral **10**:95 (May-Aug.) 1945.

An infant of 4 months suffering from pneumococcic meningitis was treated successfully with sulfadiazine and large doses of penicillin given by the intramuscular route only. Penicillin was given for seventeen days. The doses varied from 40,000 to 135,000 units daily, the total dosage amounting to 1,240,000 units. No untoward reactions occurred from the high dosage of penicillin. The authors feel that the intramuscular way of treatment is superior to the intrathecal, as it avoids severe neurologic reactions which may occur in intrathecal therapy. Such reactions were reported by Sweet and his colleagues (*J. A. M. A.* **127**:263 [Feb. 3] 1945).

Solmitz, Chicago.

Clinical Picture and Pathologic Anatomy of Hypothalamic Form of Pubertas Precox. Cornelia De Lange, Ann. pædiat. **161**:113 (Sept.-Oct.) 1943.

The author reports on 2 cases of pubertas precox. The first patient, a girl, could be observed only clinically. After pathologicoanatomic investigation of the second case and after going through the relevant literature, the author thinks it probable that this patient has had a hamartoma at the basis cerebri coming out from the tuber cinereum or damaging it.

The second observation refers to a boy with a glioma durum or an astrocytoma of the chiasma nervorum opticorum. In this case the tumor was the cause of a deficiency of ganglionic cells in the tuber cinereum, especially in the gray substance and in the nuclei tuberes.

It is supposed that the slowly growing astrocytoma in the beginning had an irritating effect and only later was the cause of destruction of ganglionic cells. So the result can be brought in accordance with the experiments on animals made by Bustamente, who by eliminating the tuber posterius of young rabbits obtained an irreversible atrophy of the gonads, and the observation of Spatz, who in a case of pubertas precox established a surplus of tuber tissue in the shape of a hamartoma as an appendage of the tuber.

Author's Abstract.

Contributions to the Neuropsychologic Studies of Epilepsy in Children: Inquiry into the Epileptic in the Service of Abnormal Infants. M. Schachter and S. Cotte, Ann. pædiat. **163**:198 (Oct.) 1944.

The examination of 118 epileptic children from 3 to 18 years of age showed severe "taint" in the following respects: (1) frequent occurrence of mental deficiency (only 7.79 per cent normal); (2) in 52 per cent of the cases, proof of previous damage to the brain; (3) teething anomalies in 47.4 per cent; (4) in 25 per cent lateness in learning to walk; (5) delayed speech development in 36 per cent; (6) late acquisition of cleanliness in 20 per cent; enuresis in 26 per cent; (7) high familial lethality and tendency of the mother to abortion; (8) in 11 per cent neurologic and in 70 per cent psychopathic symptoms.

Authors' Abstract.

The Great Toe Phenomenon in Well Older Children. J. Deutsch, Ann. pædiat. **164**:273 (May) 1945.

Of 500 children between 8 and 14 years of age who were investigated, 80 (16 per cent) showed Babinski and Oppenheim signs. This number was distributed equally between the sexes. The knowledge of this fact may help to prevent error in the diagnosis.

Author's Abstract.

Otogenic Collateral Meningoencephalitis (Ramadier). P. G. Gerlings and H. W. Struben, Nederl. tijdschr. v. geneesk. **86**:2346 (Sept. 19) 1942.

The case histories are given of 2 patients (38 and 39 years old, respectively) who showed a serious picture with meningeal and cerebral symptoms subsequent

to inflammation of the middle ear, called "meningoencephalitis collateralis" by Ramadier. The differentiation of the diagnosis of this disease and of cerebral abscess, otogenous encephalitis and otogenous hydrocephalus is discussed.

VAN CREVELD, Amsterdam, Netherlands.

HUNTINGTON'S DISEASE AND CHOREA OF HUNTINGTON. G. P. FRETS, Nederl. tijdschr. v. geneesk. **86**:2467 (Oct. 3) 1942.

The value of research on families with respect to heredity is shown for the determination of the clinical picture and for the symptoms by which it can be recognized. The example under discussion is a case which first was diagnosed as hysteria and hysterical psychosis, then as chorea of Huntington and then as schizophrenia. The conclusion, as indicated by the heredity and the anatomic examinations, is that it was a case of chronic chorea. Therefore it is necessary to speak of Huntington's disease which usually, though not always, resembles chorea of Huntington.

VAN CREVELD, Amsterdam, Netherlands.

THE PROGNOSIS FOR OTOGENIC MENINGITIS. P. G. GERLINGS, Nederl. tijdschr. v. geneesk. **87**:1417 (Sept. 4-11) 1943.

The prognosis for otogenic meningitis in recent years has become much better, owing to modern chemotherapy and improved diagnostic and operative technic. The better prognosis, especially for streptococcic meningitis, is due to chemotherapy.

In the otogenic clinic of the University of Amsterdam between January 1939 and the end of 1942 there were 30 patients with so-called primary otogenic meningitis, 14 of whom had bacterial meningitis. Of these patients 8 died (6 had a pneumococcic meningitis). The treatment consisted in repeated lumbar punctures, operation, administration of sulfapyridine and sometimes the administration of specific antipneumococcus serum.

Of the 16 patients whose spinal fluid did not contain bacteria, only 2 died.

The prognosis depends on the radical removal of the focus of infection in the temporal bone.

The endolumbar administration of sulfonamide compounds is rejected. The chemotherapy requires regular control of the blood. The ninth day episode, which now and then occurs in cases of severe disease, is indication that the treatment with sulfapyridine should be stopped.

VAN CREVELD, Amsterdam, Netherlands.

Psychology and Psychiatry

EMOTIONAL TRAUMA RESULTING FROM ILLEGITIMATE BIRTH. MANDOR FODOR, Arch. Neurol. & Psychiat. **54**:381 (Nov.) 1945.

This excellent article describes the emotional needs of children and points out the emotional trauma and resulting personality difficulties from illegitimacy because of the attitude of the mother of such children as well as "women tyrants" like an "old nurse and the wife of her guardian."

BEVERLY, Oak Park, Ill.

THEY TOO NEED SPEECH. CHARLES VAN RIPER, J. Except. Child. **12**:134, 1946.

A plea is made for the need of all handicapped children, such as the blind, the mentally retarded, the children with cerebral palsy and the deaf, to have training in the art of communication, because emotional adjustment is often obtained by verbalization. "Every handicapped person can be taught to use speech as a tool to adjust not only himself but every one else to his difference."

PALMER, Wichita, Kan.

Diseases of the Genitourinary Tract

TESTICULAR CANCER IN A TWO YEAR OLD CHILD. HERBERT STACPOOL, Bol. méd. d. Hosp. inf., México **1**:52 (May-June) 1944.

Nine months previously the right testicle began to grow, until it was about 15 cm. in length and 10 cm. in width. The left testicle was not affected. The penis was umbilicated.

Transillumination revealed an opaque tumor. The modified Aschheim-Zondek test did not reveal any gonadotropic substance in the urine. No adenopathies or metastases were noted. No abnormalities were observed. These facts were more or less against the clinical diagnosis of tumor.

The tumor was extirpated and the department of pathology reported the finding of malignant cells, the tumor being considered to be a seminoma.

MADERO, México, D. F., Mexico.

CAVITIES IN COMMUNICATION WITH THE BLADDER. H. J. BOEVÉ, Maandschr. v. kindergeneesk. **10**:311 (May) 1941.

The surgical treatment given in 3 cases of vesica bipartita and in 1 case of ureterocele in children is described. Malformations of the rest of the urinary tract were found in all 4 cases.

VAN CREVELD, Amsterdam, Netherlands.

INFLAMMATION OF THE NECK OF THE BLADDER IN CHILDHOOD. E. A. TILLEMA, Maandschr. v. kindergeneesk. **10**:410 (July) 1941.

Two girls, aged 6 and 3 years respectively, had inflammation of the neck of the bladder, a disease occurring frequently in women, but rather rarely in children.

VAN CREVELD, Amsterdam, Netherlands.

RENAL RICKETS. C. DE LANGE, Maandschr. v. kindergeneesk. **11**:33 (Nov.) 1941.

Five cases of renal dwarfism are reported. Autopsies and microscopic investigations were possible in 2 cases. In the author's opinion in renal dwarfism the underlying cause is not a chronic interstitial nephritis of unknown origin, but a malformation, a hypoplasia of the kidneys. Often the genitourinary tract also shows a congenital malformation.

The abnormal relation of the calcium and phosphorus content of the blood serum or the abnormal quantities have their influence on the growing organism. The susceptible skeletal parts suffer, but also the organs of internal secretion. It may come to an atrophy of some and to a hypertrophy (perhaps compensatory) of others—for instance, of the parathyroid gland. In one of the author's cases the adrenal glands appeared to be hypertrophic or hyperplastic.

Chown's hypothesis that a lesion of the pituitary-diencephalic mechanism is the primary cause of the syndrome called renal dwarfism could not be corroborated by the author's microscopic investigation.

In doubtful cases the fact that the polyuria in renal dwarfism undergoes no influence from products of the posterior lobe of the hypophysis may be of great value. Also abnormal broadness of the cartilagenous disks between epiphyses and diaphyses is a characteristic of renal dwarfism and not of diabetes insipidus.

VAN CREVELD, Amsterdam, Netherlands.

PROSTATISM IN CHILDREN. J. A. WEYTLANDT, Maandschr. v. kindergeneesk. **11**: 353 (Sept.) 1942.

Prostatism, the well known complex of symptoms of hypertrophy of the prostate, may also occur in women and children. The cause may be processes which by their localization in the posterior urethra increase the tone of the internal vesical sphincter or mechanically decrease its movability. Treatment may consist

in dilation of the back of the bladder, operation by punch (transurethral resection) or wedge-shaped excision from the back of the bladder by high section.

Two case reports of prostatism in young boys are given.

VAN CREVELD, Amsterdam, Netherlands.

ACUTE NEPHRITIS TREATED WITH SODIUM CHLORIDE AND ALKALI. E. LOPES CARDOZO, Maandschr. v. kindergeneesk. **12**:278 (July) 1943.

Two cases of acute nephritis in children 6 and 8 years old, respectively, are reported, demonstrating the therapeutic difficulties which may arise when acute nephritis is complicated by pneumonia. Serious disorder of the salt metabolism may occur. The treatment in both cases consisted in administration (partly parenteral) of quantities of sodium chloride and alkali.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Ductless Glands; Endocrinology

EFFECTS OF THYROID FEEDING ON OVARIAN DEVELOPMENT IN THE RAT. BENJAMIN H. ERSHOFF, Endocrinology **37**:218 (Sept.) 1945.

Female rats were raised to maturity on diets containing 0.0, 0.5 and 1 per cent desiccated thyroid. A pronounced inhibition of ovarian development was observed in thyroid-fed rats, ovaries remaining infantile both in weight and histologic appearance.

JACOBSEN, Buffalo.

THE DURATION OF ACTION OF SINGLE DOSES OF THYROID HORMONE. A. M. HUGHES, Endocrinology **37**:280 (Oct.) 1945.

There is a great deal of discrepancy between the results of various workers in regard to the rate of elimination of administered thyroid hormone. In this paper a new method of approach to the problem is described. The duration of action of single doses of thyroxin and desiccated thyroid in rats pretreated with thiouracil has been studied. Thyroxin injected subcutaneously or intravenously in solution exhibited effects for as long as equivalent doses of thyroid powder by mouth. The duration of effect increased with the size of the dose. Single intraperitoneal injections up to 50 mg. were completely metabolized within a month.

JACOBSEN, Buffalo.

THE EFFECT OF INSULIN ON THE SURVIVAL TIMES OF EVISCERATED RATS. DWIGHT J. INGLE and RUTH SHEPPARD, Endocrinology **37**:377 (Nov.) 1945.

Eviscerated rats given intravenous infusions of solution of sodium chloride died much more quickly if insulin was added to the solution. The effect of insulin in accelerating the rate at which dextrose was removed from the blood paralleled the changes in the time of survival.

JACOBSEN, Buffalo.

EFFECT OF PYRIDOXINE ON GRANULOPENIA CAUSED BY THIOURACIL. ELLA H. FISHBERG and JEFFERSON VORZIMER, Proc. Soc. Exper. Biol. & Med. **60**:181 (Nov.) 1945.

Pyridoxine (200 mg. administered orally) was given daily to 8 patients with hyperthyroidism who were being treated with thiouracil. The white cell count for the eight week period following administration of pyridoxine was 1,500 to 2,000 cells per cubic millimeter higher than during a similar period preceding its use. Three instances were cited in which pyridoxine appeared to have a distinct effect in increasing the granulocytes in patients who had leukopenia with diminution in granulocytes while receiving thiouracil. The authors suggest that the effectiveness of pyridoxine particularly because of the rapid action is due to action in the release mechanism of immature cells in the marrow. However, only exten-

sive studies of the bone marrow would determine whether or not the possibility of a direct stimulation of the myelocytic elements of the bone marrow by pyridoxine accounted for the action under these conditions. HANSEN, Galveston, Texas.

Diseases of the Muscles, Bones, Joints and Lymph Glands

AGENESIA OF THE MUSCULATURE OF THE ABDOMINAL WALL. J. C. M. VAN MARLE, Maandschr. v. kindergeneesk. **11**:27 (Oct.) 1941.

The author describes a case in which all the muscles of a girl's abdominal wall were either totally absent or were only imperfectly developed. The remarkable form of the thorax with its high sternum and inwardly bent processus xiphoideus, characteristic of this deformity, was present; at respiration the sternum was lifted up. There was also a situs abdominis inversus. The urogenital tract was probably normal in this case. VAN CREVELD, Amsterdam, Netherlands.

SOME FUNCTIONS OF THE BONE MARROW. G. M. H. VEENEKLAAS, Maandschr. v. kindergeneesk. **11**:141 (Feb.) 1942.

The author discusses the investigations of Doan, Sabin, Cunningham and Peabody on the place in the bone marrow in which the erythrocytes and leukocytes are formed. He further discusses the manner in which the cells formed in the bone marrow get into the circulation. Arguments in favor of and against the theory of Rohr (1938) on the occurrence of immature cells in the circulation are given. Finally, the author gives figures on the numbers of cells formed by the bone marrow. VAN CREVELD, Amsterdam, Netherlands.

STILL'S DISEASE, PARATYPHOID SEPSIS AND LEUKEMIA IN THE SAME PATIENT. C. SMEENK, Maandschr. v. kindergeneesk. **11**:364 (Sept.) 1942.

A boy 4 years old had Still's disease, paratyphoid sepsis and leukemia. The patient died. VAN CREVELD, Amsterdam, Netherlands.

EPIPHYSEODESIS OR EPIPHYSARY-DIAPHYSARY UNION. W. MOL, Maandschr. v. kindergeneesk. **11**:371 (Sept.) 1942.

The author gives a description of the method of Phemister for arresting the growth of one or more epiphyses of a leg which is too long, in order to make equal the length of the lower extremities. Twelve cases are described in which operations resulted satisfactorily. VAN CREVELD, Amsterdam, Netherlands.

TRANSVERSE LESION OF THE SPINAL CORD AFTER A DELIVERY TERMINATED BY EXTRACTION AT THE FOOT. C. DE LANGE, Maandschr. v. kindergeneesk. **12**:96 (Jan.) 1943.

A boy was delivered by extraction of the left foot. There was a flaccid paralysis of the lower limbs with absence of reflexes. These, however, could be elicited after a few days, and the reflexes became lively. During the whole stay in the hospital the heat regulation of the child was disturbed. The patient died at the age of 3 months from cervical adenitis and bronchopneumonia. Postmortem hemorrhages were found in the spinal meninges with a considerable amount of connective tissue. The cord showed a complete transverse lesion in the lower cervical and upper thoracic part. VAN CREVELD, Amsterdam, Netherlands.

OSTEODYSTROPHY OF UNKNOWN CAUSATION. A. VAN WESTRIENEN, Maandschr. v. kindergeneesk. **13**:85 (Feb.) 1944.

Osteodystrophy in a girl of 10 years was characterized by extensive changes in the structure of the bone, especially in the metacarpal bones. The classification of

the disease gave difficulties, but the possibility was considered that it was the beginning stage of the disease described by Ravina and Pêcher (1941) under the name of "arthromalacia, a familiar osteoligamentary disease," earlier described by Chavany and Raimbauld.

VAN CREVELD, Amsterdam, Netherlands.

TREATMENT OF MYOTONIA CONGENITA (THOMSEN'S DISEASE). A. BIEMOND, Nederl. tijdschr. v. geneesk. **87**:781 (April 24) 1943.

A family is described in which 8 cases of myotonia congenita (Thomsen's disease) occurred. Noteworthy is the fact that the patients all complained of migraine. A characteristic defect in the musculus orbicularis oculi enables one to recognize the illness soon after birth. Quinine orally administered in the form of quinine hydrobromide proved to have a good effect. Iontophoresis with quinine hydrochloride caused a transitory disappearance of the myotonia, a fact which supports the theory that quinine has a direct influence on the diseased muscles.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Eye

A VISION TEST FOR PEDIATRICIANS' USE. ALBERT E. SLOANE and J. ROSWELL GALLAGHER, J. Pediat. **28**:140 (Feb.) 1946.

A test of vision has been designed to select those children whom the pediatrician should refer to an eye specialist. This test can be given with little equipment and by an office assistant within less than five minutes. Two conditions in the eye of normal appearance which can cause difficulty are detected by this simple testing method: (1) lowered visual acuity and (2) latent refractive error (hypermetropia, "far-sightedness") in which normal vision is maintained by an excessive compensatory effort capable of producing eyestrain. It is important to test for the presence of hypermetropia because a significant refractive error may be present even though there is normal visual acuity: in those cases excessive exertion of accommodation corrects the refractive error but may cause fatigue and other symptoms.

The test is divided into two parts. Failure in the first part is sufficient for referral to an eye specialist and removes the necessity for carrying out subsequent procedures.

Part I. Visual Acuity.—A clean letter chart is hung whenever possible exactly 20 feet (609.6 cm.) from the patient, and care should be taken to prevent the patient from examining the chart before his test begins. Illumination may be obtained from a 50 watt bulb in an office floor lamp or from a spot light inserted in a ceiling socket. Effort should be made to light up the chart evenly and without glare: for more standard illumination a number of commercial illuminators are available. The eye not being tested is covered with a small cardboard square, and care is taken not to put heavy pressure on the eye. Squinting is not allowed. The smallest line of letters which can be read is recorded for each eye.

Part II. Latent Refractive Error (Hypermetropia).—The spectacles containing the plus 1.50 spheres are placed in position, and the patient closes both eyes for a few seconds. The left eye is then covered with a card, and he is requested to read the 20/20 line. This is repeated with the right eye covered. Ability to read the 20/20 line through the 1.50 spheres with either eye constitutes a failure and indicates that a sizable refractive error is present.

This brief method of examining eyes requires little time and only a small amount of inexpensive equipment and yet is efficient in selecting those children who have either diminished visual acuity or a latent refractive error (hypermetropia).

A supplementation of this test with tests of heterophoria is suggested for those who wish a more complete examination requiring more, but simple equipment. The necessity for a careful administration of the test because of its brevity and simplicity should be kept in mind.

AUTHORS' ABSTRACT.

Skin Diseases; Allergy

PENICILLIN IN DERMATOLOGIC THERAPY: REPORT OF RESULTS IN ONE HUNDRED CASES. THEODORE M. COHEN and RICHARD O. PFAFF, Arch. Dermat. & Syph. **51**:172 (March) 1945.

The authors tested 524 patients for sensitivity to penicillin ointment and found that 0.95 per cent reacted positively. Penicillin was found to be of definite value in the treatment of the following dermatologic diseases: pyodermas, especially tropical ulcer, infectious eczematoid dermatitis, moniliasis and dermatophytoses with streptococcic pyoderma.

McINTOSH, Iowa City.

CONTROL OF PEDICULOSIS. HERMAN A. SHELANSKI, HENRY FIELD SMYTH, ARNOLD M. CLARK, CHARLES A. ZELLER, WILLIAM L. PIOUS, JESS H. FRANK and FREDERICK H. KRAMER, Arch. Dermat. & Syph. **51**:179 (March) 1945.

An emulsion containing 5 per cent isobornyl thiocyanoacetate and 0.6 per cent dioctyl sodium sulfosuccinate was fonud to be superior for the treatment of head, body and pubic lice. The emulsion kills the lice and nits quickly, is easily applied to and removed from the hair. Cutaneous irritation reactions occurred in only 4 of the 6,258 patients treated.

McINTOSH, Iowa City.

FLEA BITES, PREVENTION AND TREATMENT WITH THIAMIN CHLORIDE. H. L. EDER, Arch. Pediat. **62**:300 (July) 1945.

The oral administration of 30 to 120 mg. of thiamine chloride daily for three days followed by a smaller daily dose for several weeks is suggested as an effective prophylactic measure against the bite of the California flea.

GRULEE JR., Evanston, Ill.

THE HETEROPHILE ANTIBODY REACTION IN INFANTS AND CHILDREN. JEROME DIAMOND and JOHN S. SENNOTT, J. Pediat. **27**:540 (Dec.) 1945.

The diagnosis of infectious mononucleosis has usually been based on the clinical observations, the appearance of characteristic lymphocytes in the blood and the positive antibody reaction against sheep cells, which has been one of the main diagnostic features of the disease.

This disease must frequently be differentiated from lymphatic leukemia and, as the authors noted, sometimes is difficult to differentiate from cases of acute infection of the upper respiratory tract accompanied by lymphadenopathy and lymphocytosis in infants and children.

Although most texts emphasize that the increase in titer of sheep antibodies occurs only in cases of infectious mononucleosis or after the injection of animal serums, several authors have demonstrated high titer reactions in the course of infections with pneumococci, Endameba coli and the Shiga bacillus. Because of this, the authors feel that too much stress should not be placed on the heterophile antibody reaction alone in making the diagnosis of infectious mononucleosis.

In a group of cases of acute infection of the upper respiratory tract in St. Louis during the winter of 1944-1945, routine heterophile agglutination tests were made. Control tests were given children without infections at the same time.

Seventeen children in a group of 118 had titers of over 1 to 160, the upper border of normal for the method used, which was a modification of Davidsohn's technic. The maximum agglutination was 1 to 2,560. In the control group of 38 cases, only 1 child had a titer of 1 to 320.

The authors feel that too much stress should not be placed on the diagnostic value of the heterophile antibody reaction in infectious mononucleosis without the presence of the abnormal lymphocytes found in the disease. Also, a standardized technic should be adopted by various institutions for running heterophile agglutination tests in order to interpret better the results obtained.

In the group of cases presented with an increase in heterophile reactions above the accepted normal, it was felt that perhaps the sulfonamide drugs used in these cases might possibly have altered the reaction although, as has been mentioned previously, high positive titers have been reported in other infections.

AUTHORS' ABSTRACT.

HEREDITARY SKIN DEFECT IN THE NEWBORN INFANT. PAUL FREUD, ADRIAN W. RHODES and ALBERT WEISZ, J. Pediat. **27**:591 (Dec.) 1945.

The authors give a detailed description of a hereditary defect of the skin, mentioning the extent and location of the lesion. They discuss the mechanism leading to defects and review 128 cases in the literature. They comment on prognosis and treatment of the condition and add a case of their own. In this case they observed a defect of the same size and location on the scalp of mother and child, proving its hereditary origin.

AUTHORS' ABSTRACT.

ACRODYNIA. N. I. HEYBROEK, Maandschr. v. kindergeneesk. **12**:163 (March) 1943.

Since now and then, as a result of the correspondence of the symptoms of pellagra and acrodynia, similar treatment for both diseases is recommended, the author begins by pointing out the differences between these diseases. He gives the history of 2 cases of acrodynia; in neither was success seen from treatment with nicotinamide, whereas Bellergal (a preparation of gynergin, bellafolin and phenylethylbarbiturate) gave symptomatic improvement.

VAN CREVELD, Amsterdam, Netherlands.

Miscellaneous

SEDATIVES AND STIMULANTS IN PEDIATRIC PRACTICE. HARRY GOLD, J. Pediat. **27**:546 (Dec.) 1945.

The use of drugs for stimulation or depression in children has received relatively little attention in the pediatric literature and textbooks. The basis for their use in children seems to be drawn largely from experience with adults. That tendency in drug therapy is clearly revealed in the matter of dosage. The dose for children is often stated in terms of the adult dose divided by a number. The indications are clear that the child is not merely a fraction of an adult, but something different, with a relatively greater surface area, more rapid basal metabolism, a large liver and high excretion of urine. There is need for more systemic studies of the action of drugs in children.

The common experience that children require relatively larger doses of sedatives than adults does not necessarily indicate that they are more tolerant; the sedatives given children are often employed as chemical restraints, and for this purpose adults also require large doses. The common statement that infants and children are more susceptible to morphine is not well supported and is based on the accidents which have resulted from the use of unduly large doses. A dose of 0.02 to 0.03 mg. per kilogram of body weight is effective against cough, and doses of 0.25 mg. or less per kilogram are effective against pain. As to the barbiturates, there seems to be little evidence of qualitative differences in their actions. Phenobarbital, because of its longer duration of action, is the most favored preparation for most purposes of sedation and sleep.

The so-called "stimulants" are pharmacologically more heterogeneous, and the drug which is used depends on a decision as to what system needs to be

stimulated, the cerebral cortex, the respiratory center, the vasomotor center or the peripheral blood vessels. Strychnine, camphor and alpha-lobeline are of no therapeutic value. Caffeine is of no value as a cardiac stimulant and is inferior to other analeptics to depression by narcotic poisons. For vasomotor stimulation by a peripheral constriction of the blood vessels, an intramuscular dose of 0.1 mg. of neo-synephrine hydrochloride, or of 0.2 mg. of paredrine (para-hydroxy-alpha-methylphenylethylamine) per kilogram is the treatment of choice. Metrazol and nikethamide are of no value as cardiac stimulants, but useful as central vasomotor and respiratory stimulants, in doses of 2 mg. per kilogram intramuscularly of metrazol and 5 mg. per kilogram intravenously or intramuscularly of nikethamide. Picrotoxin is the drug of choice as an analeptic for barbiturate poisoning and is given in doses of 0.2 mg. per kilogram intramuscularly every fifteen minutes until signs of excitation appear. The digitalis glycosides should be reserved for the cases of heart failure.

AUTHOR'S ABSTRACT.

THE USE OF SULFAMERAZINE IN INFANTS AND CHILDREN. GILBERT B. FORBES, ANNE PERLEY and JEAN DEHLINGER, J. Pediat. **28**:24 (Jan.) 1946.

A study of the absorption, methods of administration, therapeutic effectiveness and toxicity of sulfamerazine in an unselected group of 135 infants and children with infections revealed the following pertinent data:

1. Sulfamerazine is rapidly absorbed from the gastrointestinal tract and rather slowly excreted by the kidney. Accordingly, adequate concentrations in the blood are easily attained by the oral administration of 0.05 Gm. per kilogram of body weight every eight hours (three quarters of the total daily dosage usually employed with sulfathiazole and sulfadiazine). Sulfamerazine thus possesses an advantage over the other sulfonamide drugs in that they must be given in larger total dosage with more frequent doses to attain comparable levels in the blood.

2. High concentrations in the blood are easily and rapidly produced by the subcutaneous administration of sodium sulfamerazine. The absorption of sulfamerazine from the gastrointestinal tract, although more rapid and complete than is the absorption of the other sulfonamide drugs, does not lead to values sufficiently high to obviate the need for parenteral administration of the drug when extremely high values are desired.

3. Sulfamerazine was observed to pass into the spinal fluid to the extent of from 52 to 83 per cent of the whole blood value and 41 to 73 per cent of the plasma value, while the concentration in pleural and ascitic fluid equaled that in the plasma.

4. From a purely clinical evaluation, the therapeutic effectiveness of sulfamerazine is entirely comparable to that of sulfapyrazine, sulfadiazine and sulfathiazole.

5. The toxic reactions encountered were relatively frequent but for the most part were mild, and no serious reactions occurred. On the basis of the authors' past experience, the frequency of toxic reactions was definitely greater with the use of sulfamerazine than with sulfapyrazine and certainly as great as with sulfadiazine.

AUTHORS' ABSTRACT.

THE PREVENTION OF EDEMA IN INFANTS UNDERGOING SULFONAMIDE THERAPY. ROBERT KLEIN, J. Pediat. **28**:37 (Jan.) 1946.

Sudden gains of a pound (453.6 Gm.) or more in weight, as well as the appearance of clinical edema, had been noticed fairly frequently in infants treated with sulfonamide drugs for many infections. It was considered that the edema might be due to retention of sodium because of the administration of alkalis containing the sodium ion along with the sulfonamide drugs.

Infants given the sulfonamide drugs in the Children's Hospital were divided into unselected groups. One group received sodium bicarbonate, while a second

group was given potassium citrate as its adjuvant alkali. Sodium lactate was later used to show the lack of importance of the anion. A mixture of the potassium citrate and the sodium bicarbonate was also tried.

It was found that there were considerably fewer cases of edema in the group receiving potassium-containing alkali than in the group who were given an alkali containing the sodium ion. It was also found that the dosage of the various alkalis was dependent on the amount of cation present, which was of course to be expected.

Of 23 patients given 0.28 to 0.42 Gm. of sodium bicarbonate (0.0033 to 0.005 gram molecule of cation) per kilogram of body weight, 6 became edematous; of 11 patients given 0.48 Gm. of sodium lactate (0.0043 gram molecule of cation) per kilogram of body weight, 2 became edematous; of 31 patients given 0.44 to 0.70 Gm. of potassium citrate (0.004 to 0.006 gram molecule of cation) per kilogram of body weight, none became edematous, and of 23 patients given 0.42 Gm. of potassium citrate and 0.21 Gm. of sodium bicarbonate per kilogram of body weight, 3 became edematous.

No advantage for the potassium-containing alkali was proved in older children, as clinical edema was not a problem in this group. Clinically noticeable pitting edema with a sudden and appreciable gain in weight was seen in all patients listed as being edematous. Mention was made of the advantages of potassium-containing alkalis in treatment of nephrotic patients with infections and of patients with cardiac decompensation. The latter use was reported in the *New England Journal of Medicine* by Ohnysty and Wolfson.

The possibility of potassium intoxication in cases of anuria was brought up, although the doses advocated were much smaller than those found in the previous reports of potassium poisoning in anuria. However, renal diseases per se were not thought to be a contraindication to the use of potassium-containing alkalis.

The nitrazine method of testing the p_H of the urine was used, and the alkalis used satisfactorily maintained a p_H of 7 to 7.5 or better. However, in those patients who became edematous the edema frequently appeared with the urine at a p_H of less than 7. The urine would tend to become more alkaline when the edema subsided. In 1 case the edema disappeared while the infant was still being given sodium bicarbonate. In the others, the sodium-containing alkali was stopped with or without the substitution of potassium citrate.

AUTHOR'S ABSTRACT.

INCIDENCE OF REACTIONS TO SULFONAMIDE DRUGS IN INFANTS AND CHILDREN. HERBERT WILLIAM FINK and CLEMENT A. SMITH. J. Pediat. **28**:40 (Jan.) 1946.

Records of the number and type of reactions to sulfonamide drugs were kept during a two and one-half year period at the Children's Hospital of Michigan. During this period, in which at least 5,000 infants and children received sulfonamide medication, 60 instances of drug fever (25 accompanied by rashes), 2 of malignant neutropenia, 2 of hemolytic anemia and 4 of anuria (2 fatal) were encountered. The total percentage of untoward reactions was thus less than 1.4. In a separate series of 1,500 patients studied for important urinary changes, significant hematuria occurred in 10, or less than 1 per cent.

Sulfadiazine was used in the majority of both series. Striking differences between the number of reactions to this drug and to sulfathiazole or sulfamerazine were not apparent. In all administrations the usual dose of about 0.14 Gm. in each twenty-four hours per kilogram of body weight was employed, and alkalis were not administered concomitantly.

Hematologic complications of drug therapy were usually associated with fever and rash. All febrile, cutaneous and hematologic reactions ceased after cessation of administration of drugs. Fifty-nine per cent of the patients who reacted once to sulfonamide compounds showed immediate reactions to later repetitions

of the same drug—usually with only one dose of 0.26 Gm. Since such responses appeared only in patients known to have reacted to previous administration, it is concluded that there is no danger of "sensitizing" a child by an uncomplicated course of sulfonamide therapy. Moreover, in view of the small percentage of reactions of all sorts, the authors conclude that the standard drugs of this series are certainly as well tolerated by pediatric patients as by adults, if not, indeed, better.

Of 7 children known to be reactors to one sulfonamide drug, a trial dose of a different drug of the same series produced reactions in only 2, and neither of these reacted to a third sulfonamide drug.

Cutaneous tests of infants and children suspected to be sensitive to sulfonamide drugs with sulfonamide-containing human serum did not demonstrate sensitivity with the accuracy of oral testing with a single dose. AUTHORS' ABSTRACT.

EFFECTS OF PROLONGED IRRADIATION OF MICE WITH FLUORESCENT LIGHT. B. E. KLINE and H. P. RUSCH, Proc. Soc. Exper. Biol. & Med. **60**:254 (Nov.) 1945.

In view of the carcinogenic property of ultraviolet radiation in experimental animals and the possible relation of sunlight to cutaneous cancer in man, the authors studied the effect of prolonged exposure to the daylight fluorescent lamp. Two groups of 48 strain C male albino mice 2 to 3 months old were exposed to the rays of a Westinghouse "Daylight" Mazda F fluorescent lamp. Liquid petrolatum U.S.P. was applied to the ears of one group of animals; however, no evidence of carcinogenesis developed, nor did erythema or irritation of the cornea appear. Although the total amount of radiant energy was considerable the intensity of ultraviolet radiation in the 3,125 angstrom band was low.

HANSEN, Galveston, Tex.

CONCENTRATION OF SULFAPYRIDINE AND SULFANILAMIDE IN BLOOD AND FLUID, AND THE EFFECT ON THE HEMOGRAM. J. S. VAN DER HORST, Maandschr. v. kindergeneesk. **10**:384 (July) 1941.

A study was made of the concentration of sulfanilamide and sulfapyridine in the blood of children suffering from pneumonia and nontuberculous meningitis. The dosage of the drugs was 100 mg. per kilogram of body weight for pneumonia and 150 to 200 mg. per kilogram of body weight for meningitis. In the blood of children recovering from pneumonia the mean concentration was 2 to 3 mg. per hundred cubic centimeters, and the concentration in the blood of those recovering from meningitis was 3 to 4 mg. per hundred cubic centimeters. During meningitis, the concentration in the spinal fluid was always found to be more than 50 per cent of the concentration in the blood. The spinal fluid never contained the acetylated form of the drug.

A report was made of the hemogram during treatment with sulfanilamide and sulfapyridine, based on the data on all children treated with these drugs in the Children's Hospital of Rotterdam from 1938 to June 1941. Decline of granulocytes occurred especially when the number of leukocytes was normal before the beginning of the therapy, without leukocytosis and shift to the left. Steady attention to the hemogram is necessary, as unexpected falls in the number of granulocytes occur even after twenty-four hours. VAN CREVELD, Amsterdam, Netherlands.

LEAD INTOXICATION COMPLICATED BY FLORID RICKETS IN A BABY. T. JANSSEN, Maandschr. v. kindergeneesk. **11**:338 (Aug.) 1942.

Janssen reports a case of lead poisoning in a 5 month old infant who completely recovered. A series of roentgenograms showed that the lead lines in the skeleton for the greater part disappeared during complicating active rickets.

VAN CREVELD, Amsterdam, Netherlands.

SALICYL INTOXICATION IN A BABY. L. M. DOYER, Maandschr. v. kindergeneesk. **11**:361 (Sept.) 1942.

A case is reported of salicyl intoxication in a baby which was treated for erythema neonatorum with a powder containing 33 per cent salicyl compound.

VAN CREVELD, Amsterdam, Netherlands.

INTOXICATION FROM BEECHNUTS. M. VAN EEKELEN, C. DEN HARTOG and P. J. VAN DER LAAN, Nederl. tijdschr. v. geneesk. **87**:831 (May 1) 1943.

The Dutch newspapers have asked their subscribers for information about cases of intoxication caused by eating beechnuts. Three hundred and thirty-one persons have written that they have been poisoned in this way, but undoubtedly this is only a part of the real number of cases. Two hundred and twenty-three cases could be compiled statistically. The percentage of old persons and of women was greater than that of children and of men. Thirty-nine per cent were poisoned by eating less than fifty nuts. The symptoms appeared quickly, usually within two hours, and consisted of nausea, headache, dizziness, pain in the stomach and the abdomen, diarrhea and a paralyzed, tired and weak feeling in the limbs, with a tendency toward fainting. Three patients became unconscious. All patients recovered quickly, the majority of them within twenty-four hours. Sometimes the diarrhea continued for some days.

VAN CREVELD, Amsterdam, Netherlands.

THE QUADRUPLETS IN ZWOLLE. G. J. VAN LOOKEREN CAMPAGNE, Nederl. tijdschr. v. geneesk. **87**:1176 (June 26-July 3) 1943.

The way in which the quadruplets in Zwolle, the Netherlands, were successfully treated during the first two months of life is described.

VAN CREVELD, Amsterdam, Netherlands.

Book Reviews

A Future for Preventive Medicine. By Edward J. Stieglitz, M.D., F.A.C.P. Studies of the New York Academy of Medicine Committee on Medicine and the Changing Order. Price, $1. Pp. 77. New York: The Commonwealth Fund, 1945.

This little book should appeal to pediatricians. Dr. Stieglitz boldly offers "consideration and recommendations as tentative suggestions" on the "probable future application of preventive medicine," and declares that pediatricians and obstetricians are the only practicing physicians who have actively applied their art and knowledge. His discussion of "definitions" is stimulating.

The chapter "Health Over the Last Forty Years" illustrates his argument without belaboring the available statistics. The remainder of the book is largely devoted to developing the concept of "constructive medicine" that is familiar to the pediatrician who succeeds in teaching parents to care for their children and who knows the numerous agencies and disciplines concerned with "the en masse approach to preventive medicine."

He emphasizes that "health is not an inalienable right. It is a privilege. Privileges invariably entail equivalent responsibilities. . . . Nature grants few rights, preferring to demand that privileges be earned. Health, like freedom and peace, continues only as we exert ourselves wisely to maintain it." Yet his approach is constructive, and he indicates education as "the most significant task facing those concerned with wholesale or en masse preventive medicine."

He says, in connection with the proposal "to give health to the people by means of legislation," that the true responsibility to society is to make available the means by which health may be pursued and conserved, remembering that the individual citizen must accept considerable personal responsibility.

He stresses the need for more medical research and for liberal support of research with public moneys, which must not be politically controlled. He points out why periodic medical examinations have fallen into disrepute and suggests the term "health inventory" as descriptive of a more comprehensive and expensive service of individualized analysis and synthesis.

Bioenergetics and Growth, with Special Reference to the Efficiency Complex in Domestic Animals. By Samuel Brody, Ph.D., Chairman, Committee on Growth and Energy Metabolism, College of Agriculture, University of Missouri. With a foreword by M. F. Miller, Director, Missouri Agricultural Experiment Station. A Publication of the Herman Frasch Foundation. Price, $8.50. Pp. 1023, with many tables and charts. New York: Reinhold Publishing Corporation, 1945.

This volume serves to integrate many studies relating to nutrition, growth and efficiency of metabolism. Vast amounts of data concerning the physiology and biochemistry of nutrition have been assembled, and the author has interpreted the information in an interesting and effective manner. Despite the broad scope of the fields discussed and the interspersion of many charts and tables, the reader's attention is carried easily from chapter to chapter without abatement of interest. Each of the twenty-five chapters deals with a distinct aspect of nutrition, such as: the definition and description of the nutritional units, the manner in which each serves its function, factors relating to the efficiency complex and the manner in which all agencies are integrated toward the maintenance of homeostasis, or dynamic biologic balance throughout the whole organism. The author reviews thoroughly the nature of growth in general, for regions as well as for the total

organism. Consideration is given to the extension of the laws of growth of the person to the growth cycle of social aggregates. Several chapters are devoted to the economics of work and to the production of milk, eggs, meat and wool. The final chapter not only summarizes the work as a whole but develops a rational philosophic approach toward the processes of life.

From the space the author devotes to the discussion of studies using farm animals as subjects one might assume that the work had been designed primarily for the agricultural economist or for other nonmedical readers. The substance of the volume makes such a conclusion unwarranted. It should prove highly valuable to the physiologist, the nutritionist or the physician as a source of information, orientation and reference.

Pulmonary Tuberculosis. A Handbook for Students and Practitioners. By R. Y. Keers, M.D., and B. G. Rigden, M.D. With a foreword by F. H. Young. Price, $5. Pp. 273, with 124 illustrations. Baltimore: Williams & Wilkins Company, 1945.

Although the incidence of tuberculosis in infancy and childhood and the usual types of the disease encountered in those age periods are referred to, the authors are concerned primarily with pulmonary tuberculosis in the adult. They emphasize, throughout, the importance of considering the patient as a whole in his emotional and intellectual acceptance of his infection and in relation to his socioeconomic background. The authors are respectively the senior physician and medical superintendent and the first assistant medical officer of the Tor-na-Dee Sanatorium.

After a brief review of the development of the understanding of tuberculosis and short chapters on the bacteriologic and pathologic factors of the disease, there is a detailed discussion of the taking of the history and of the physical and roentgenologic examination of the patient. The rationale of rest in bed is explained, and collapse therapy, or thoracoplasty, is considered in all phases, with many illustrative roentgenograms. The advantages of treatment in a sanatorium over care at home are shown to be manifold; chiefly to be mentioned are the availability of a thoracic surgeon and a bronchoscopist and the freedom from the worry and emotional conflicts of the home. The responsibility of the physician for the patient who returns to society after the disease has been arrested is also stressed.

The book is written for the student and the general practitioner. The aim seems to be to develop throughout the medical profession an appreciation of how great is the probability of arresting the disease when modern facilities and knowledge are employed and to enable the individual physician to recognize the disease as early as possible and to cooperate to the full with the specialist and with governmental and private agencies for its control.

Cardiomegaly and Cardiac Insufficiency of Early Infancy. By J. Bonaba, J. R. Marcos, M. L. Saldun de Rodríguez and J. A. Soto. Price, not given. Pp. 150, with 32 illustrations. Montevideo, Uruguay: Editorial J. García Morales, 1945.

In this much needed monograph the authors have undertaken to bring together the scattered clinical and pathologic literature on this subject and to organize it in utilizable form, using as illustrations 50 cases of their own.

In the authors' classification, modified from Kugel, the following categories are considered: (1) congenital anomalies; (2) infections; (3) anemias; (4) syndrome of myocardial degeneration of Kugel and Stoloff; (5) hypertrophies of metabolic cause, including those caused by disorders of glands of internal secretion, vitamin deficiencies, storage diseases and cardiomegaly in newborn babies of diabetic mothers; (6) tachycardia; (7) hypertension; (8) tumors of the heart; (9) exudative pericarditis, and (10) an unclassified group.

Each of these categories is discussed in detail with illustrative cases.

A general clinical, electrocardiographic and roentgenologic discussion is then given with tables of differential diagnosis of the general syndrome of infantile cardiac insufficiency from pneumonia and pericarditis. It might be considered a weakness of the latter half of the book that, after earlier consideration of the different pathologic conditions causing the syndrome, the etiologic classification is rather neglected and a purely clinical one utilized, the presence or absence of murmurs and cyanosis being used. This is probably inevitable in the present state of clinical diagnosis of these conditions. A useful and critical discussion of the roentgenologic methods of determining the size of the heart in infants is included.

In treatment, the authors are firmly convinced of the value of digitalis and bleeding. More detail as regards dosage in relation to weight would be desirable in this chapter.

The book is a valuable addition to the literature on the subject of heart disease and deserves the consideration of all those interested in this phase of pediatrics.

Fundamental Patterns of Maladjustment: The Dynamics of Their Origin. By Lester Eugene Hewitt and Richard L. Jenkins, M.D. Price, not given. Pp. 109, with 33 tables and 1 illustration. Springfield, Ill.: State of Illinois, 1946.

This is a statistical analysis based on 500 records of cases of children examined at the Michigan Child Guidance Institute. The material was gathered by social workers, psychologists and psychiatrists. The patients were "problem children" from various parts of the state of Michigan, who were referred by school authorities, courts and welfare agencies.

The authors concluded that there are three fundamental patterns of maladjustment; namely, the syndrome of unsocialized aggressive behavior, the syndrome of socialized delinquency and the syndrome of overinhibited behavior. Each of these patterns is identified and characterized by a group of traits. The first pattern, for example, is characterized by assault tendencies, intiatory fighting, cruelty, defiance of authority, malicious mischief and inadequate feelings of guilt.

The authors attempted to determine the situations at home which gave rise to the various patterns described but it is difficult to understand their conclusions, based, as they are, on a large number of cases, but with insufficient information about each case. The important factor "parental rejection," for example, was apparently determined by observations of the social workers and not by detailed study of the parents by a psychiatrist.

This study represents a large amount of work. Since it is statistical, most readers will have to take the results for granted. The style of writing is technical and not easy to follow.

Estudios sobre la alimentación del lactante [calostro, leche humana, mezcla láctea, heces del lactante]. By Professor Pedro Escudero, Ministerio del interior—Dirección nacional de salud pública. Price, 10 pesos. Pp. 487, with illustrations. Buenos Aires: Instituto nacional de la nutrición, 1944.

This collection of reprints of research work done by Professor Escudero and his colleagues of the National Institute of Nutrition of the Argentine Republic is divided into four parts: (1) studies on colostrum, (2) studies on human milk, (3) Escudero's milk mixture and (4) feces of the nursing infant.

The studies on colostrum and on human milk are interesting, demonstrating variations in composition of human milk not generally appreciated. These workers have also demonstrated a definite effect of the diet of the mother on the composition of her milk.

Escudero's milk mixture is a formula for use when mother's milk is absent. It is made up of calculated proportions of homogenized cow's milk, white sugar and either lard or homogenized cream in a cereal water base and is frequently acidulated with lactic acid. The research on the formula, both in the laboratory

and clinically, is well done and proves the mixture satisfactory. However, to any one familiar with artificial feeding in pediatric practice in the United States, it hardly bears the stamp of originality.

The format makes the book difficult to read and repetitive. Nevertheless, for the student of nutrition it presents a wealth of chemical, microscopic, bacteriologic and clinical data and will serve well as a reference source.

Roentgen Diagnosis of Diseases of the Gastrointestinal Tract. By John T. Farrell Jr., M.D., Clinical Professor of Radiology, Graduate School of Medicine, University of Pennsylvania. Cloth. Price, $5.50. Pp. 271, with 193 illustrations. Springfield, Ill.: Charles C Thomas, Publisher, 1946.

This book presents a concise, fundamental guide to roentgenologic diagnosis of gastrointestinal disease. Fluoroscopic and roentgenographic methods are considered with regard to applicability, mediums and position of the patient. The layout of this book is especially interesting and practical. The "Standard Nomenclature of Disease" is used for the order of presentation. A brief outline of each condition is given under the headings "contour," "motility" and "position"; this is followed by a discussion of pathologic changes, symptoms and methods of roentgen diagnosis. By these means, the differential diagnosis is simplified.

Emphasis is given to the relative importance of roentgenologically recognizable diseases by the styles of type used. This unique arrangement indicates which are illustrated and discussed, which are discussed without illustrations, and which are merely listed. The illustrations are numerous and well chosen.

As the author states in the preface, this book was written as a manual, not a reference work. As such, it will be of greater value to the student and "occasional roentgenologist" than to one who practices this specialty. A large volume of material is covered briefly but adequately. The sections devoted to foreign bodies are especially well treated. Dr. Farrell has written a book which should be valuable in its field. Although there is no new material included, the style and method of presentation are especially worth while.

Group Psychotherapy: Theory and Practice. By T. W. Klapman, M.D. Price, $4. Pp. 344, with 14 illustrations. New York: Grune & Stratton, Inc., 1946.

Although group psychotherapy has been used for a long time, a scientific approach to the problem is comparatively recent. Its importance has increased with the recognition of the present day problems of psychotherapy. In this volume the author reviews the literature and summarizes the views of the other practitioners and also his own extensive experience in this type of psychiatry.

The book is divided into three parts: The first part discusses the history and origin of psychotherapy; the second analyzes the basis for therapy with the reeducational aspects and the interrelationship between group and individual psychotherapy, and the third part discusses methods and use of psychotherapy in outpatient departments, hospitals and private practice. There is a chapter on psychotherapy for children which points out its use by teachers and in the management of problem children.

The book contains many illustrations. Discussions with patients and groups of patients are given verbatim. It is written in a clear, understandable style. It is one of an enlarging series of contributions to this old subject, which is fairly new from a scientific standpoint.

Bronconeumonia en la Infancia. By Enrique Sujoy. Pp. 169, with 53 illustrations. Price, unknown. Buenos Aires, Argentina: El Ateneo, 1945.

This book contains a rather complete review of bronchopneumonia in infancy. It is clearly printed on heavy paper and contains many black and white illustrations, as well as a few in color. The diagrams and photomicrographs are excep-

tionally clear. A brief history of the subject is given in chapter 1. This is followed in chapters 2 to 18 by competent discussions of the etiologic, bacteriologic, pathologic and clinical features of the condition. There are numerous reproductions of roentgenograms, demonstrating more clearly than usual the extent and location of the pneumonic processes.

The author's observations are based on 468 cases of bronchopneumonia following pertussis, measles, diphtheria and "grippe." He has found repeated transfusions of whole blood to be the most effective treatment, but has not had satisfactory results with sulfonamide compounds. Vaccine therapy has been found ineffective in all types of the disease.

This is undoubtedly a good reference book on the subject for those abie to read Spanish.

A Bibliography of Infantile Paralysis. By Ludvig Hektoen, M.D., and E. M. Salmonsen. Price, $15. Pp. 672. Philadelphia: J. B. Lippincott Company, 1946.

This exhaustive bibliography of infantile paralysis is arranged according to years, beginning in the year 1789 and running up to the present time. The abstracts are numbered and consist of a total of 8,320. In addition to the abstracts there are an author's index and a subject index.

This is the most comprehensive consideration of the sort that the reviewer has ever seen. It must be as complete as is humanly possible to make it. It should be a model for any further publication of a like nature on any other disease. That it should prove extremely useful not only as a standard but from the practical side of medicine goes without saying. It is a most valuable book of a unique type.

The Modern Attack on Tuberculosis. By H. D. Chadwick, M.D., and A. S. Pope, M.D. Second edition. Price, $1. Pp. 134, with 5 illustrations. New York: The Commonwealth Fund, 1946.

Two of the nation's best phthisiologists have condensed into this small handbook of some 120 pages the essential parts of present day concepts of tuberculosis. First the development of the modern methods of attack on the disease is discussed. This is followed by an interesting chapter on epidemiology. The authors list five outstanding discoveries which have greatly contributed to knowledge of tuberculosis. These are Auenbrugger's demonstration of percussion, in 1761; the invention of the stethoscope by Laennec; Koch's discovery of the tubercle bacillus, in 1882, and of tuberculin, and Roentgen's discovery.

The knowledge and the tools are at hand, the authors believe, completely to eradicate tuberculosis, perhaps, within a couple of generations. All that is required is their effective application. Methods of case finding, organization of programs for community campaigns for control of tuberculosis and the role of the sanatorium in control and treatment are carefully discussed.

Perhaps public health officials and public health nurses may find the greatest use for the information contained in the handbook, but all physicians whose work brings them in contact with tuberculous patients will find it a quick source of much useful information. The book is highly recommended.

News and Comment

NOTICE

Application Fee for the American Board of Pediatrics, Inc.—Because of the increased cost of running the American Board of Pediatrics, Inc., the Board has found it necessary to raise the application fee to $125, effective May 1, 1947.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-General: Dr. L. Emmett Holt Jr., 477 First Ave., New York 16.

Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto 2.
Secretary: Dr. S. G. Ross, 1390 Sherbrooke St. W., Montreal.
Place: New York. Time: July 14-17, 1947.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

Save the Children International Union

President: Mrs. Gordon Morier.
Secretary: Dr. Georges Thélin, 43 Quai Wilson, Geneva, Switzerland.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

Associação Paulista de Medicina, Secçaõ de Pediatrias

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Luiz Augusto Monteiro Toledo, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.
Time: Twelfth of every month, 8:30 p. m.

British Paediatric Association

President: Prof. G. B. Fleming, 13 Lynedoch Crescent, Glasgow.
Joint Secretary: Prof. Alan Moncrieff and Dr. Donald Paterson, Hospital for Sick Children, Great Ormond St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Nederlandische Vereeniging voor Kindergeneeskunde

President: Dr. J. L. Keyzer, 114 St. Josephstr., Tilburg.
Secretary: Dr. H. Reerink, 2B Paul Krugerstr., Arnheim.
Place: Children's Hospital or Pediatric Clinic. Time: Three times a year.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. L. F. Meyer, 29 Toelsohn St., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASES IN CHILDREN

President: Prof. Norman Capon, 49A Rodney St., Liverpool, England.
Secretary: Dr. J. N. O'Reilly, 46 Harley St., London W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

SOCIEDAD BOLIVIANA DE PEDIATRIA

President: Dr. Ernesto Trigo Pizarro.
Secretary: Dr. Carlos Ferrufino, Casilla 272, La Paz, Bolivia.
Place: La Paz, Bolivia.

SOCIEDAD CUBANA DE PEDIATRIA

President: Dr. Teodosio Valledor, Habana.
Secretary: Dr. Carlos Hernandez Miyares, Hospital Nuestra Señora de las Mercedes L y 21, Apartado 2430, Habana.
Place: Cátedra de Clinica Infantil, Hospital Nuestra Señora de las Mercedes y Hospital Municipal de Infancia, Habana. Time: Last Wednesday of every month.

SOCIEDAD DOMINICANA DE PEDIATRIA

President: Dr. Alberto Peguero, Ciudad Trujillo, R.D.
Secretary-Treasurer: Dr. Jaime Jorge, Ciudad Trujillo, R.D.
Place: Children's Ramfis Hospital. Time: 8 p. m., last Thursday of every month.

SOCIEDAD ECUADORIANA DE PEDIATRIA

President: Dr. Francisco de Icaza Bustamente.
Secretary: Dr. M. I. Gómez Lince, P. O. Box 693, Guayaquil.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Luis Berlanga Berumen, Bucareli No. 85, Altos, Mexico.
Secretary: Dr. Jésus Alvarez de los Cobos, Ignacio Mariscal 124, Mexico.

SOCIEDAD DE PEDIATRÍA DE CÓRDOBA

President: Dr. Juan Francisco Herrera, Córdoba, Argentina.
Secretary: Dr. Bernardo Serebrinsky, Dean Funes 2000, Esq. Ocaña (N.), Córdoba, Argentina.
Place: Comite pro Defenso del Niño, Dean Funes 2000, Córdoba, Argentina. Time: Once a month.

SOCIEDAD DE PEDIATRIA DEL LITORAL

President: Dr. Jose E. Celoria, Hospital Centenario, Rosario, Argentina.
Secretary: Dr. Gloria Lovell, Hospital Centenario, Rosario, Argentina.

SOCIEDAD DE PEDIATRÍA DE SANTIAGO DE CUBA

President: Dr. Antonio Béguez César, Sagarra 107, Santiago de Cuba.
Secretary: Dra. Susana Texdó Vaillant, Padre Pico 57, Santiago de Cuba.
Place: Colegio Médico. Time: Last Tuesday of every month.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Dr. Pedro J. Alvarez.
Secretary: Dr. Ernesto R. Figueroa, 3a Avenida 10, Bella Vista, Caracas.
Place: Hospital Municipal de Niños Jose Manuel de los Rios, Caracas.

Société de Pédiatrie de Paris

President: Dr. Leveuf, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Maladies, 149 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

Swedish Medical Society, Section for Pediatrics and School Hygiene

President: Prof. Arvid Wallgren, 53 Strandvägen, Stockholm.
Secretary: Dr. Henning Magnusson, 58 Odengatan, Stockholm.
Place: Various clinics and hospitals in Stockholm and Uppsala. Time: Second Friday of each month (except summer).

Uruguayan Society of Pediatrics

President: Dr. Jose Bonaba, Montevideo.
Secretary: Dr. Héctor Fossatti, Durazno 1882, Montevideo.
Place: Club Medico del Uruguay, Avenida Agraciado 1464 (Piso 13), Montevideo.

NATIONAL

American Medical Association, Scientific Assembly, Section on Pediatrics

Chairman: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.

American Academy of Pediatrics

President: Dr. Jay I. Durand, 515 Cobb Bldg., Seattle, Wash.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.

American Hospital Association, Massachusetts Hospital Association

Chairman: Dr. Frank Wing, Boston.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly 79, Mass.

American Pediatric Society

President: Dr. Harold K. Faber, 2361 Clay St., San Francisco.
Secretary-Treasurer: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12.

Canadian Society for the Study of Diseases of Children

President: Dr. H. S. Little, 300 Dufferin Ave., London, Ontario.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, 67 College St., Toronto 2.

Society for Pediatric Research

President: Dr. Mitchell I. Rubin, 219 Bryant St., Buffalo 9, N. Y.
Secretary: Dr. Robert Ward, Bellevue Hospital, New York 16.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Wesley H. Anderson, 2404 Washington Blvd., Ogden, Utah.
Secretary-Treasurer: Dr. F. M. Kriete, State Capitol, Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Secretary-Treasurer: Dr. Charles D. May, 300 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Three meetings a year, occurring from September to May.

North Pacific Pediatric Society

President: Dr. Percy Guy, 502–2d Ave., Seattle, Wash.
Secretary: Dr. Aldis B. Johnson, 515 Cobb Bldg., Seattle, Wash.

Northwestern Pediatric Society

President: Dr. George Kimmel, Redwing, Minn.
Secretary-Treasurer: Dr. Northrop Beach, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Rocky Mountain Pediatric Society

President: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver 2.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Stewart H. Welch, 117 S. 20th St., Birmingham 5, Ala.
Secretary: Dr. W. Ambrose McGee, 1601 Monument Ave., Richmond 20, Va.

STATE

Alabama Pediatric Society

President: Dr. Jerome C. Chapman, 2160 Highland Ave., Birmingham.
Secretary-Treasurer: Dr. Ruth Berrey, 2021–6th Ave. N., Birmingham.

Arizona Pediatric Society

President: Dr. W. P. Sherrill, 342 W. McDowell Rd., Phoenix.
Secretary: Dr. W. F. Schoffman, 926 E. McDowell Rd., Phoenix.
Place: Phoenix or Tucson. Time: At time of state meeting.

Arkansas State Pediatric Association

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco 9.
Secretary: Dr. Chester I. Mead, 1930 Truxton Ave., Bakersfield.

Florida State Pediatric Society

President: Dr. Councill Rudolph, 103–5th St. S., St. Petersburg.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association convention and fall meeting.

Georgia Pediatric Society

President: Dr. Alton Johnson, 102 E. Central Ave., Valdosta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Place: Atlanta. Time: At time of annual state meeting.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. David Gaberman, 1179 Allyn St., Hartford, Conn.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.

Illinois State Medical Society, Section on Pediatrics

Chairman: Dr. Gerard N. Krost, 2376 E. 71st St., Chicago.
Secretary: Dr. Frederick H. Maurer, 331 Fulton St., Peoria 2.

Indiana State Pediatric Society

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Matthew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.
Secretary-Treasurer: Dr. James Dunn, 414 Blackhawk Hotel, Davenport.

Louisiana State Pediatric Society

President: Dr. S. George Wolfe, 1560 Line Ave., Shreveport.
Secretary-Treasurer: Dr. W. C. Rivenbark, 1448 Louisiana Ave., New Orleans 15.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn, N. Y.
Secretary: Dr. George R. Murphy, 292 Madison Ave., New York.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary: Dr. P. F. Lucchesi, Philadelphia Hospital, Philadelphia.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Donald J. Barnes, 3001 W. Grand Blvd., Detroit, Mich.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.

Mississippi State Pediatric Society

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

Nebraska Pediatric Society

President: Dr. Paul N. Morrow, 1614 Medical Arts Bldg., Omaha 2.
Secretary-Treasurer: Dr. Michael Crofoot, 1407 Medical Arts Bldg., Omaha 2.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

New Mexico State Pediatric Society

President: Dr. M. K. Wylder, 221 W. Central Ave., Albuquerque.
Secretary-Treasurer: Dr. Ly Werner, 221 W. Central Ave., Albuquerque.

North Carolina Pediatric Society

President: Dr. Charles R. Bugg, Professional Bldg., Raleigh.
Secretary: Dr. Charles F. Williams, 817 Hillsboro St., Raleigh.

Northern California Pediatric Society

President: Dr. Edith M. Meyers, 431–30th St., Oakland.
Secretary: Dr. A. L. Gleason, 411–29th St., Oakland 9.
Place: San Francisco. Time: Second Thursday of February, April, September and November.

Oklahoma State Pediatric Society

President: Dr. J. B. Snow, 625 N. W. 10th St., Oklahoma City.
Secretary: Dr. Bertha Levy, 1200 N. Walker St., Oklahoma City.
Place: With Oklahoma State Medical Association. Time: Annual Meeting.

South Carolina Pediatric Society

President: Dr. George D. Johnson, Spartanburg.
Secretary-Treasurer: Dr. B. O. Ravenel, Roper Hospital, Charleston.

Tennessee Pediatric Society

President: Dr. F. T. Mitchell, 376 S. Bellview, Memphis.
Secretary-Treasurer: Dr. W. O. Vaughan, 2103 Hayes St., Nashville 5.
Time: Second Monday in April.

Texas Pediatric Society

President: Dr. Max Woodward, 202 N. Travis St., Sherman.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas 4.

Virginia Pediatric Society

President: Dr. Emily Gardner, 1100 W. Franklin St., Richmond 20.
Secretary: Dr. Louise Galvin, 214 S. Boulevard, Richmond 21.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. Jack Basman, 1021 Quarrier St., Charleston.
Secretary: Dr. Harry E. Baldock, Medical Arts Bldg., Charleston.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. I. Hartman, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. Alexander N. Freed, 2012 W. 25th St., Cleveland.
Place: Cleveland Medical Library Bldg. Time: 8:15 p. m., October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. J. H. Ebbs, 13 Queen's Park, Toronto, Canada.
Secretary: Dr. J. F. McCreary, 170 St. George St., Toronto, Canada.
Place: Academy of Medicine. Time: 8:30 p. m., third Thursday of each month.

Baltimore City Medical Society, Pediatric Section

Chairman: Dr. Charles O'Donovan Jr., 5 E. Read St., Baltimore.
Secretary: Dr. T. Campbell Goodwin, 16 E. Biddle St., Baltimore.

Bronx Pediatric Society

President: Dr. Harry S. Pizer, 1726 Davidson Ave., New York.
Secretary: Dr. Nathan M. Greenstein, 1488 Metropolitan Ave., New York.
Place: Morrisania City Hospital. Time: 8:30 p. m., second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Lambert Krahulik, 14 Sidney Pl., Brooklyn.
Secretary: Dr. Joseph Battaglia, 713 Bushwick Ave., Brooklyn 21.
Place: Granada Hotel. Time: 8:45 p. m., fourth Wednesday of February, March, April, May and November.

Buffalo Pediatric Society

President: Dr. Douglas P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo 9, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

Central New York Pediatric Club

President: Dr. Arthur W. Benson, 2 St. Paul St., Troy.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and October.

Chicago Pediatric Society

President: Dr. Joseph Greengard, 4753 Broadway, Chicago 40.
Secretary: Dr. Alvah L. Newcomb, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May inclusive.

Cincinnati Pediatric Society

President: Dr. Leo S. Friedman, 666 Rockdale Ave., Cincinnati 29.
Secretary: Dr. George Renner, 3144 Jefferson Ave., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dallas Pediatric Society

President: Dr. O. René Caillet, 4325 Cole Ave., Dallas, Texas.
Secretary-Treasurer: Dorothy Wyvell, Bradford Memorial Hospital for Babies, Texas.
Place: Children's Medical Center. Time: 1 p. m., third Saturday and 8:30 p. m., the first Thursday of each month.

Detroit Pediatric Society

President: Dr. Otto Grob, 651 Fisher Bldg., Detroit 2, Mich.
Secretary: Dr. Harold B. Rothbart, 773 Fisher Bldg., Detroit 2, Mich.
Place: Variable. Time: Third Wednesday of each month.

Houston Pediatric Society

President: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd., Houston, Texas.
Place: River Oaks Country Club. Time: 7:30 p. m., fourth Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1624 Professional Bldg., Kansas City.
Secretary: Dr. Leland Speer, 1022 Parkway, Kansas City.
Place: Kansas City General Hospital. Time: On call.

Knoxville-Oak Ridge Pediatric Society

President: Dr. Henry S. Christian, 205 Medical Arts Bldg., Knoxville, Tenn.
Secretary: Dr. John Eggleston, Oak Ridge Hospital, Oak Ridge, Tenn.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Albert L. Hill, 1401 S. Hope St., Los Angeles.
Secretary-Treasurer: Dr. Robert Simonds, 1925 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Henry Rascoff, 895 Eastern Parkway, Brooklyn.
Secretary: Dr. Harold Levy, 750 St. Marks Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. Meyeron Coe, 217-02-91st Ave., Queens Village, N. Y.
Secretary-Treasurer: Dr. Louis Appel, 143-42 Cherry Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION ON PEDIATRICS

President: Dr. John Washington, 2203 Wyoming Ave., Washington, D. C.
Secretary-Treasurer: Dr. George Maksim, 1418 Good Hope Rd. S.E., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., third Thursday of October, January, March and May.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Barton Etter, 1024 Madison Ave., Memphis, Tenn.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. R. P. Showalter, 411 E. Mason St., Milwaukee 2.
Place: Milwaukee Children's Hospital. Time: Second Wednesday in February, April, June, October and December.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. Robert O. Du Bois, 122 E. 76th St., New York.
Secretary: Dr. Harold W. Dargeon, 1095 Park Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from November to May, inclusive, 8:30 p. m.

OKLAHOMA CITY PEDIATRIC SOCIETY

President: Dr. J. B. Snow, 625½ N. W. 10th St., Oklahoma City.
Secretary: Dr. Bertha Levy, 1200 N. Walker St., Oklahoma City.
Place: Oklahoma Club. Time: Third Thursday of each month.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Arthur M. Dannenburg, 235 S. 15th St., Philadelphia 2.
Secretary: Dr. D. Stewart Polk, Rosemont, Pa.
Place: College of Physicians, 19 S. 22d St. Time: 8:30 p. m., second Tuesday from October to May, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. Elwood Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh 13.
Place: Pittsburgh Academy of Medicine. Time: Second Friday in October, December, February and April.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Edwin L. Kendig Jr., 828 W. Franklin St., Richmond 20, Va.
Secretary-Treasurer: Dr. Thomas S. Chalkley, 1200 E. Broad St., Richmond, Va.
Place: Medical College Hospital. Time: 8 p. m., third Thursday of each month, except June, July and August.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. William L. Bradford, 260 Crittenden Blvd., Rochester 7, N. Y.
Secretary-Treasurer: Dr. Donald D. Posson, 222 Chili Ave., Rochester 11, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee.
Time: Third Friday of each month from October to May.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Joseph C. Jaudon, 337 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Gilbert B. Forbes, 500 S. Kingshighway, St. Louis 10.
Time: Second Thursday of each month from October to May, inclusive.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Norman W. Murphy, 1300 Madison St., Seattle 4.
Secretary: Dr. David M. Harris, 630 Medical Arts Bldg., Seattle 1.
Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Robert J. Dostal, 710 Wilshire Blvd., Santa Monica, Calif.
Secretary: Dr. H. M. Van Dyke, 541 E. Broadway, Long Beach, Calif.
Place: University Club of Los Angeles. Time: 6:30 p. m., first Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Park Bradshaw, Muskegon, Mich.
Secretary: Dr. Harry A. Towsley, 1313 E. Ann St., Ann Arbor, Mich.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRICS SECTION (NEW YORK)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.
Place: Hospitals of Westchester County. Time: Third Thursday in November, January, March and May.